MAKING BODIES COMMENSURATE: THE SOCIAL CONSTRUCTION OF HUMANS, ANIMALS, AND MICROBES AS OBJECTS OF SCIENTIFIC STUDY

by

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The road to this dissertation has been long and winding. To be sure, this is not where I thought I was heading when I entered graduate school eight years ago. At that time I intended to use my training in anthropology to return to the field of global health and transnational clinical trials, working to improve the methodological issues in these studies that were the impetus for my decision to undertake a degree in anthropology in the first place. But in between, life happened. The process of graduate school is not an easy one, as anyone who has been through it can attest. The best laid plans often go awry, and this was more than true for me.

During my time in graduate school I have been exposed to the social study of complementary and alternative medicine which changed the ways in which I think about science, objectivity, the scientific method, and the role of society in all aspects of knowledge creation. My mind has been opened to social theories that at first glance had nothing to do with studies of medicine, but that I now see have everything to do with them! I took jobs that provided me with opportunities to develop and hone my qualitative research skills and transformed me from a clinical interviewer into an empathetic witness. And perhaps most importantly, I learned that despite my best efforts to believe otherwise, place and space matter. I uprooted myself from a lucrative career in the soggy Pacific Northwest to a near pauper-like existence in the desert Southwest. I struggled those first years just to survive and adapt to my surroundings, much like the animals and vegetation that call this place home. But I did not give up, and as I surrendered to my surroundings, and let the desert be my guide, a series of magical accidents started to happen.

Through them, I found that the most important place is the home I create for myself, the place where I am most at peace but that simultaneously sets my heart and spirit on fire. For me, this was "the animal turn," and surrendering to a deep, visceral need to work with animals and on issues that concern them, our relationships to them, and the animal-human-environment triad. This realization came late in my life to be sure, and also late in my graduate career. Not wanting to switch fields of study, I needed to find a way to incorporate this passion into the work I had already done. With help from a loving, sympathetic group of friends who encouraged me at every turn to "follow my inner animal nutter….but maybe not too, too much" and a very supportive committee, I found a way to marry my passions with my training. I now embark on what I hope will be a long, interesting, and challenging career in the anthropology of animal-human studies.

This dissertation has benefitted from the thoughtful and constructive guidance of so many mentors and the loving and generous friendship of so very many, near and far. I am indebted to the scientists, individuals, activists, and experts who generously gave their time to speak with me and share their thoughts, insights, and experiences. In particular, dog study participants welcomed me into their homes and in some cases, their families. I am so very grateful for the gift of your friendship.

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Because this dissertation encompasses work that includes Japan, I would be remiss if I did not mention those that first opened this world to me. The Elkhorn Rotary Club sent me to Japan at age 16 as an exchange student for one year. It was there my love of anthropology blossomed, and in reality, where the seeds for this whole adventure were planted. Who knew?! Jean and John Henderson, you were my mentors for that year abroad, and you have continued to champion my successes ever since. Your friendship means so much and I look forward to spending more time with you next year in our beloved Sconnie! And to Yamada-Sensei and my Japanese family, the Kitanakas: here I find that words truly fail me. You were there through so much, and you have continued to be an ever present and supportive force in my life. Thank you will never be enough, and yet it is all I have. Honto ni, domo arigatou gozaimashita!

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Ivy, your friendship is one of the best gifts I have received from this graduate experience. We have shared so many wonderful belly laughs that sometimes I forgot PhD school was supposed to be serious business! Your guidance through independent studies on biology and biocultural anthropology has been instrumental in my development and you have challenged me to think about things in new ways and to never sell myself short. Mentors like you are far and few between, and I am so honored to have had your guidance, both professional and personal, at such a critical juncture in my life.

Stacey, you are such an inspiration!! Your passion for the environment, animals, and teaching are, I believe, unparalleled in our department. I have benefitted immeasurably from this by working with you on the Palm Oil Awareness Initiative. In particular have learned so much from watching you navigate difficult situations while engaging the issue from a passionate and yet always scientifically grounded standpoint. I am a better scientist because of you. The feedback you have provided on my dissertation has been some of the most constructive and important I have received, I am beyond grateful. I look forward to many more years of friendship and collaboration.

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sure I took breaks for walks, treats, and naps. You reminded me to smell the creosote and listen to the birds sing. How did I ever get so lucky?

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Dedication

This dissertation is dedicated to:

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ABSTRACT

This dissertation utilizes three independent research projects to examine one overarching theoretical question: **How do people understand, contest, negotiate, and / or rationalize the ways in which bodies – human, animal, and microbial - are socially constructed as commensurate, or not, in science?** Using three unique projects focusing on either the human, animal, or microbial body, this dissertation broadly explores the social processes inherent in the construction of "bodies" for scientific research. This dissertation explores the complexity of how bodies are used in science, how this is understood by individuals, and the impacts this has not only on science but also the intertwined lives of animals, humans, and their microbes. Each paper explores a key set of questions drawing from a shared set of theoretical lenses, including local biology and biolooping, commensuration, the biovalue of bodies, and the microbiome. Specifically this dissertation presentation will explore these questions: 1) How are Japanese bodies socially constructed as different from other bodies in ethnobridging clinical trials?; 2) How is local biology employed as a technique of commensuration at the site of the Japanese body, by the government, and the global pharmaceutical industry and what does this mean for scientific studies utilizing it in this way?; 3) How do scientists construct nonhuman primates as appropriate proxies for humans in biomedical research experiments?; 4) How do individuals understand themselves and their health in relation to pet dogs and microbes?; and 5) How do humans understand the ways in which humans, animals, and microbes co-create their biological and social worlds?

This dissertation shows how the construction of the body as an object of scientific study is negotiated, contested, and taken up in daily life, and how this is flexible, malleable, and not at all uniform. It explores the ways in which biomedical knowledge of the body is socially constructed and how it co-creates the animal, microbial, environmental, and cultural worlds in which it circulates. Through doing so and using techniques and lenses grounded in biosocial anthropology, this dissertation adds to the literature on the body in both medical and multispecies anthropology.

INTRODUCTION

Background

"*Kimu no taishitsu ga tsuyoi desune!"* I first heard this phrase as a high school Rotary exchange student to Osaka, Japan in 1991. Little did I know then the impact this phrase and the way it expresses different cultural views of the body and medicine would have in terms of shaping my life's work. *Taishitsu*, loosely translated, means "one's innate constitution," and to my Japanese friends and family, mine was *"tsuyoi"*, very strong and robust. I was rarely sick, had a healthy appetite, and was always active in some kind of sport or ready for outdoor adventures. As such, my innate constitution according to my Japanese family was strong and unbending, something to be admired from the standpoint of Japanese views on health and wellness. I did have one problem, however: acne. And my admittedly very bad case of cystic acne was difficult to treat and had been for years. The fact that it seemed to be getting worse in Japan was something that my host mother, Etsuko, a kind, warm, and generous woman, found very distressing. To some extent, she took my pimples' resistance and flare-ups as a personal attack on her cooking! This is because unlike most Americans, the Japanese have very strong beliefs and behaviors around the idea of food as medicine and food as the most important and basic aspect of one's health. Thus, in an effort to tame my acne, Etsuko went out of her way to make foods for me that she thought would help decrease inflammation in my system and counteract my acne. As my acne continued to get worse, however, she and my host father, an ear, nose, and throat surgeon, sought the help of a fellow Rotarian, a dermatologist. Dr. Tanimoto prescribed a very bitter, powdered medication that I took

daily for several weeks, unfortunately to little avail. As my acne continued to worsen, they puzzled over my case, trying to determine whether they should continue with the medication and increase my dosage or switch to a different medication that could be imported from overseas. As I later learned, the medication the doctor was giving me was a formulation that had been developed by a Japanese pharmaceutical company and was not marketed outside Japan. My host family and Dr. Tanimoto believed that as an American, my *taishitsu* was very different from that of Japanese individuals, and therefore the medication was not strong enough to work for me. The best solution then, was to find a medication that had been developed specifically for a foreign *taishitsu*, and as such, was not available as a marketed drug in Japan.[1] Eventually my (American) parents sent a high dose antibiotic from the United States prescribed by our family physician which very measurably improved my acne. By that time, however, this experience had piqued my awareness of and interest in ideas of bodily similarity, difference, and the ways in which culture intersects with health, illness, and medicine.

At the age of 25 I embarked on a career in international public health, and began working in the field of international vaccine clinical trials. The organization for which I worked, PATH, was moving into neglected and tropical vaccine development as well as engineering several devices for the delivery of vaccines and medicines in low-resource settings. This field seemed to offer an ideal vantage point from which to explore the ways in which culture, society, medicine, technology, and beliefs about the body are incorporated into the production of scientific and medical knowledge. The scientist in me

[1] Japanese doctors are able to procure drugs that are available in overseas markets in certain cases, and my host parents as well connected Rotarians with strong international ties would have had access to such medications. Today this is an issue of much contention in the Japanese medical system as drug development takes years, and often drugs that have been available for over ten or twenty years elsewhere are still not available in the Japanese market.

became increasingly interested in this work and with the support of my direct supervisor who felt it was a good fit for me, I pursued a certificate in clinical research coordination from the University of Washington. Soon, I began working on several international, multi-sited drug and device projects for PATH.

Having studied Japanese and travelled throughout much of Southeast Asia for a decade by the time I arrived at PATH, the majority of my work assignments were in Asia. This is important because Asian ideas of the body had by now permeated many of my own ideas of the body, health, disease, and our connections with the natural world. A strong awareness of and deference to bodily difference plays a central role in the indigenous medicine systems in these countries. Individuals' constitutions (i.e. *taishitsu*) are important aspects of how health, wellness, and illness management are approached in the traditional medicine systems of Asia, including Kampo (Japanese medicine), Ayurveda, Traditional Chinese Medicine, and Hangul (Korean medicine), among others. My life experiences in Asia instilled in me an intrinsic appreciation for these ways of knowing, understanding, and treating the body, at the center of which are the ideas that no two bodies are the same, and bodily difference matters.

While at PATH, I oversaw the implementation of four large, Phase 3 randomized controlled trials (RCTs) of vaccines in the Philippines, India, and Sri Lanka as well as a Phase 2 RCT device trial in China. Over the course of the seven years I spent managing these outsourced trials, I became increasingly uncomfortable with the ways in which the clinical trials were being both conducted and described. Of particular concern to me was the way in which, especially in the Phase 3 RCTs, all of the subjects were treated the same, regardless of the life worlds they inhabited. The idea that bodily difference exists

between peoples across time and place and are strongly connected to both internal (i.e. individual) and external (i.e. cultural, environmental, dietary, etc.) influences, was absent from the ways in which these RCTs were being conducted. In clinical trials, bodies - regardless of where they are located or their unique histories, are largely treated as the same, and constructed in such a way that any difference is mediated out by sophisticated techniques and exclusionary policies. I wondered why scientists were not paying more attention to the many things that make us uniquely different and which could be having profound effects on the ways medicines were being responded to in different populations. Aside from the interest in the role that genetics play in the development of drugs, there is really no interest in incorporating nuanced differences between individuals into RCTs. Humans are biosocial animals, and the micro- and macro-environments we inhabit are dynamic, fluid, and constantly changing. Moreover, we interact, communicate, and adapt to myriad human and nonhuman agents. Why then did the science I was involved in seek to flatten all of the context, nuance, and complexity of human life into a one dimensional view of reality? What were the consequences of decontextualization and the generic construction of human life on the scientific process?

An epiphany came to me at pivotal moment in my career as I was reading over edits the principal investigator (PI) had made to a manuscript I drafted about the results of a recent multi-sited clinical vaccine trial. The trial examined the safety and efficacy of co-administering the Japanese encephalitis (JE) and measles vaccines, and had been conducted in Manila, Philippines. I was particularly troubled to read these two sentences that the PI had inserted into the article: "Measles seroprotection rates in 9-month-old infants have varied widely in developing countries. Our high rates are similar to those in

populations from Oman, Indonesia, and a number of African countries, and may reflect the good nutritional status of the infants and the strict attention to cold chain maintenance and monitoring in this study" (Gatchalian et. al. 2008). Two things gave me pause over these sentences. First, and foremost, we had collected *zero* data from any of the infants in the study on their nutritional status, and therefore knew nothing about whether or not they might have had nutritional supports that would have facilitated greater immunogenicity or seroprotection rates than in other children. Second, as the only member of the team who had visited the study sites many times over the course of several years, I knew that it was highly likely that the children in Manila actually had a *lower* nutritional status given that the majority of them came from very poor families who lived in or near slum areas. During my visits to the Manila study site, study nurses and staff from the clinical research organization hired to monitor the study shared many of the participants' stories and backgrounds with me. I learned that many, if not most of the children had participated in the study because it gave them access to the JE vaccine, something that was not available via the national health system and that was prohibitively priced if purchased privately. Despite the high cost, many parents wanted their children protected from this disease, especially because they often traveled to visit family in remote parts of the Philippines where mosquito borne illnesses are epidemic.

Another issue of concern was that the scientific heads of this study were frequently discussing data from the Philippines site when in discussion with other scientific experts, funders, pharmaceutical representatives, and leaders at the World Health Organization and UNICEF, with very little attention to the context in which it was

collected. And this could have provided important clues as to the ways in which children's bodies were responding to the vaccine.

For example, children in all three arms of the study had baseline seroprotection levels against measles that were between sixteen and twenty-one percent, suggesting some sort of natural and/or inherited protection from their mothers. Seroprotection rates against JE disease were much lower, but still present at between three to six percent. At the end of the study, the only group that hadn't reached 100% seroprotection against measles was the group that received the vaccines simultaneously, which was also the group that had the highest baseline seroprotection levels. Rates of seroprotection against JE following the study ranged from 90-92% for all of the groups. Given that these children all showed some protection against both of these diseases prior to the study, it could have been very useful to know where this protection came from. Were these children gaining natural protection against measles and JE from their mothers who had been vaccinated or perhaps even been exposed to the disease at some point in their lives? Was it possible that children themselves had some natural exposure to JE, either in Manila or when traveling to a rural area? If the children weren't exposed through their mothers, where was the exposure coming from and did it matter in terms of how children responded to these vaccines? Was there a response difference in children who were exposed via their mothers versus those who weren't (i.e. those whose exposure was much lower than 20%, with a seroprotection of around 10% at the base of the confidence interval)? Understanding just some of the context of these children's and their families' lives, as well as their mothers' vaccination, travel, and illness history, could have provided useful information to help explain why those with higher baseline

seroprotection against JE responded slightly more poorly to the vaccine than those with lower rates at baseline did, and why those with the highest levels of seroprotection against measles at baseline showed the lowest seroprotection after vaccination.

However, discussions about this study among experts made it seem as if it had been collected in a vacuum and from a population that was uniquely homogenous and uniform. Vitally important elements related to geography, environment, and the social lives of study subjects were being wholly ignored. For example, the Filipino children in this study lived in a densely packed, polluted city located at sea level. Their parents were from lower socio-economic backgrounds, and many had moved to the city from remote parts of the Philippines to find work. As such, they were economically and socially marginalized, living in slums without consistent access to electricity, clean water, and sanitation facilities and often faced food insecurity. It is likely that their nutritional status was not only poor, but that they had also been impacted by the biological implications and imprinting of their parents' low socioeconomic status throughout the life course (McEwan 2003; Flynn 1999). Any one of these factors could have had a significant impact on the main endpoint of the study, children's seropositivity rates for both JE and measles at one month and a year following vaccination. Taken together, along with other biological issues that were ignored including mothers' immunogenicity status, parents' smoking status, caffeine intake and so forth, seemed akin to the gerrymandering of science, in which study designs yield results lacking in the rich color, fragrance and complexity of the human experience. More importantly, however, by ignoring these important contextual clues, it is possible that investigators missed an opportunity to more

fully understand the ways in which children mount responses to disease and how protection against these diseases can be further enhanced in vaccination programs.

I had come to believe strongly that the way in which we were "doing" science was not only avoidant of those very things we sought to impact, but that in fact we might actually be doing greater harm than good. I therefore began to seek ways in which to address the questions that I could no longer hold back from asking and which my training in international studies, public health and administration, and clinical trials had left me ill equipped to answer. These questions led me to the field of medical anthropology where I have been encouraged to study biocultural ways the body is experienced in health and sickness, and to critique the ways humans and animals are constructed for clinical trials as a matter of practice glossed as objective and scientific.

It is important to note here, that while I left the field that I now critique, I do so as someone who has been awed by the power of clinical trials and RCTs[2] as techniques of knowledge production while being attentive to their limitations. These studies generate data which are significantly productive in that they improve, change, and save human lives. Were it not for clinical trials and RCTs, biomedicine and science would be very different fields and the effects on human society great and far reaching. Therefore, what I aim to do in this dissertation is not attack evidence-based medicine, population medicine, or those scientists and doctors who construct it. Rather I seek to draw attention to the

[2] It should be noted that randomized controlled trials (RCTs) and clinical trials are not the same thing. For example, RCTs are the gold-standard of biomedical research and they are used in this dissertation to denote those studies that employ a randomized, double-blind controlled design to guard against participant and investigator bias. I use the term clinical trials to denote studies that are not necessarily RCTs. Many such studies exist where a double-blind, controlled design would not be feasible or ethical. The Dogs as Probiotics study is one such example. As such, I use both these terms throughout the dissertation, but believe it is important for the reader to understand that there is, in fact, a very real and discernable difference between the two.

limitations of various dimensions of these studies which are not only problematic from a scientific standpoint but also health and safety. I aim to draw attention to the elements of clinical trials and RCTs that are missing, namely the complexity and subtle nuances that can add texture to a one-dimensional picture. To be clear, I am also not saying that incorporating these elements into study designs is simple or the silver bullet that will solve all of the fields' problems. If this were the case, I am sure that the many well-meaning, profoundly ethical, and truly talented individuals working in this field would have incorporated these elements. On the contrary, they are messy, convoluted, highly charged, and often problematic. They are the human elements of science. Anthropology has a strong role to play, and this dissertation will contribute to anthropology's involvement through providing examples of how using biocultural lenses can help us improve this field for all involved.

In what follows, I briefly provide an overview of each of the chapters in this dissertation. Each chapter is a stand-alone paper that has been or will be published. In each separate paper overview I describe how the paper fits into the dissertation as a whole and introduce the lenses I specifically use in that paper. Following this overview of the chapters I describe the four key lenses that are used not only to explore the issues each paper is focused on, but which tie these papers together into a cohesive examination of the biocultural construction of bodies – human, animal, and microbial – in biomedicine. Lastly I describe the methods and sampling used in each of the projects in greater detail. This is done so that the reader might understand not only the methods as they pertain to each paper, but how each paper is part of a larger project, and each project

part a program of research conducted over the eight years I spent in training as a medical anthropologist.

Three Papers: Exploring Human, Animal, and Microbial Bodies in Science

This dissertation utilizes three independent research projects to examine one overarching theoretical question: **How do people understand, contest, negotiate, and / or rationalize the ways in which bodies – human, animal, and microbial - are socially constructed as commensurate, or not, in science?** The main objectives of this research are three-fold:

1) To explore the ways in which individuals understand, interpret, and situate the use of various bodies – human, animal, and microbial - in biomedical research.
2) To examine the ways in which individuals justify the use of bodies as proxies for other bodies in science.
3) To investigate how individuals' interpretations and justifications of the use of various nonhuman bodies as proxies for human ones in science impacts their everyday behaviors and interactions with these nonhuman bodies.

In using three separate research projects, I was able to explore the social construction of "bodies" from a broader perspective than if I simply looked at the commensuration of human-human or animal-human bodies in clinical trials. Rather, by taking an example from each of these, a more holistic understanding begins to come into relief, one that allows us to really begin to understand the complexity of the ways in which bodies are used in science, how this is understood by individuals, and what impact this may have on not only science, but the intertmingled lives of animals, humans, and their microbes.

Each of the papers addresses its own key questions, which tie back to these overall objectives. In "Politics of Local Biology, Ethnobridging Studies in Japan," I ask

how are Japanese bodies socially constructed as different from other bodies such that an entirely unique way of testing drugs has been developed around the Japanese notion of difference. In what ways is local biology employed as a technique of commensuration at the site of the body, by the government, and the global pharmaceutical industry and what does this mean for scientific studies utilizing it in this way? In "Flexible (In)Commensurability: The Social Process of Constructing Animals as Lab Experiments," I examine the ways in which scientists construct non-human animals (hereafter referred to as "animals") as proxies for humans in biomedical research experiments. Given that so much concern is paid to ensuring that human-human differences are flattened in human clinical trials, this paper seeks to understand how animals are constructed as appropriate stand-ins for humans in biomedical science. This paper specifically looks at the work that scientists do in creating animals as proxies for humans, although the larger research project itself looked at the intersection of scientists and lay persons and how each makes sense of, justifies, and ultimately negotiates the use of animals as proxies for humans in biomedical research. Lastly, "Pets and the Human Microbiome: Dogs as Probiotic Delivery Systems" asks how do individuals understand themselves and their health in relation to pet dogs and microbes? How do humans understand the ways in which humans, animals, and microbes co-create their biological and social worlds? This paper is the result of ethnographic data collection within a larger clinical trial that sought to examine the impact of pet dogs on the microbiota of elderly individuals.

Overview of Papers

Paper One: *The Politics of Local Biology in Transnational Drug Testing: Creating (Bio)Identities and Reproducing (Bio)Nationalism Through Japanese "Ethnobridging" Studies*

In beginning my dissertation work, I was drawn to explore the ways in which standardized clinical trials collapsed individuals down to a few similar characteristics in order to make generalizations about the effectiveness of a medication for society at large. In exploring these issues in the sphere of multinational clinical trials for global pharmaceuticals, I turned to Japan, the place that first piqued my interest in many of these issues. As noted above, Japanese ideas of human bodily similarity are vastly different from those in other parts of the world. Thus, this became the focus of the first paper in my dissertation. For the Japanese, the Western ways of doing clinical research are problematic, given that they conflict with notions of what it is to "be Japanese" and their belief that Japanese people are, in fact, biologically unique in their brains and bodies. Because of this, an entire system of testing drugs intended to be marketed in Japan has been developed to ensure that specific testing is conducted on biologically and culturally Japanese bodies prior to a drugs' entrance in Japan. This system, commonly referred to as "ethno-bridging studies" is unique because it aims to provide data on the efficacy, safety, dosage or dose regimen used in a geographic region where the drug was not previously studied. Using data from this region and data from other studies in other regions, scientists can then extrapolate how a drug will perform in this new geographic region. However, in Japan, it is rarely this simple. There, drugs are often required to go through the entire drug development process again, using Japanese bodies. This is different for every other nation which generally requires little to no testing in specific ethnic or racial groups prior to marketing approval. For most other nations' governmental regulatory

bodies that oversee pharmaceutical approvals, data sets taken from larger clinical trials that included various minorities in their study populations are considered good enough for approval.

Implicit in the Japanese insistence on ethnobridging studies are ideas about what constitutes a "purely" Japanese body that can be understood in relation to nationalism, bio-identity, and local biology. Interestingly, at a cursory level it may appear that ethnobridging studies are an attempt to incorporate many of the things that I often felt lacking in clinical research described above, especially in terms of local biology. However, upon further examination, it becomes clear that ethnobridging studies are actually missing the key point of local biology, which is the continual feedback loop between what is termed "intrinsic" (i.e. race, gender, age, disease) and "extrinsic" factors (i.e. environmental factors such as climate, diet, and culture). Clinical research thus treats these various factors that have important and dynamic intersecting effects on one another as if they are static elements able to be isolated and examined in a vacuum.

Paper Two: "*Flexible (In)Commensurability: The Social Process of Constructing Animals as Lab Experiments*

In examining the ways in which this process is engaged in Japan, it awakened my curiosity toward how we define bodily similarity and difference and what impact this has on the drug development process, science, biomedicine, and society's understanding of these intersections. I began to wonder: if an entire industry has developed to ensure that Japanese uniqueness and bodily difference are taken into account in transnational drug testing, how then do we understand the ways in which other species of animals are used as the basic building blocks for human drug development? Thus, I extended my inquiry from the ways in which the human body is constructed and utilized as a mode of

knowledge production in scientific research, to also include the ways in which other animal bodies come to be interpolated into proxies for human bodies in biomedical research.

In Paper two, I explore the ways in which scientists construct nonhuman primates (NHPs) as simultaneously both commensurable and incommensurable for humans. Commensuration is the social process by which different qualities are transformed into a common metric (Espeland and Stevens 1998:314). Commensurability is a useful lens through which to understand how seemingly very different objects can be collapsed down to a few, often very basic, common characteristics, and thus transformed into objects that can be compared. The concept is one of the pivotal aspects of any clinical trial where study subjects are selected upon a tightly defined set of characteristics that then allows investigators to attribute any changes that occur to the study drug or device and not to differences between the study subjects. In the case of animal studies that will provide the basic data for further study of a drug in humans, it is a very instructive lens through which to view how animal bodies become proxies for human ones. This is because while on the surface it may seem like investigators are simply making determinations on which animals to use based on biological and physiological similarities with humans, a closer examination reveals the complexity within which scientists operate and their role in the social construction of animal proxies for humans in biomedical sciences. It shows the invisible work scientists do to illuminate the similarities between humans and other animals and how they are variously demarcated as separate. This is, then, the focus of the second paper, "Flexible (In)commensurabilities," which is based on research I conducted between 2012-2014. In this paper I explore how scientists and lay persons understand,

interpret, negotiate and/or contest the ways in which NHPs are made to be proxies for humans in biomedical research.

At the time I conducted this research, a debate around the issue of the use of NHPs in biomedical research was flaring in the United States. At that time, only the US and Gabon allowed biomedical research on chimpanzees. In 2013, the NIH placed 310 of its research chimpanzees into retirement, such that they would no longer be able to be used for biomedical experiments. Fifty chimps remained available in case of "emergencies" such as an ebola or similar outbreak where chimps might be the best model in which to test treatments and/or vaccines. However, in late 2015, the NIH announced that it would retire the remaining fifty chimps under its care and end all funding to research programs using chimpanzees. Importantly, this did not extend to other NHPs, only the great apes and primarily the chimpanzee, as it is most commonly used in biomedical research. Reasons for this change, as noted by the head of the NIH at the time and based on a report by the Institutes of Medicine (IOM), were that very little research conducted using chimps had yielded important outcomes for human health (Altevogt et. al. 2011). It should be noted, however, that this is much disputed by proponents of the continuation of chimpanzee use in biomedical research, including many of the scientists in my sample. Additionally, much of the focus of discussion among the public and scientific experts was on the biological, physiological, and social similarities between chimpanzees and humans. Unlike other NHPs, we share more than 98% of our DNA with chimpanzees and almost all of our genes (Prufer et. al. 2012). Theoretically, this makes them ideal candidates for understanding how drugs might work in humans. On the other, however, they also share many social and behavioral similarities to humans,

such that many people including scientists, lay persons, ethologists, and government officials now believe that it is inhumane and unethical to do experiments on them. But given that other NHPs are not afforded the same protections chimpanzees now enjoy under US law,[3] and are used widely throughout biomedical research, it begs the question: how do we construct animals as similar but *just different enough* to be used in biomedical research experiments? The political and social atmosphere during that period made an ideal backdrop in which to conduct this work as it was at the forefront of many news stories and facebook posts, and as such, often on the minds of scientists, the public, and activists.

Paper Three: *Pets and the Human Microbiome: Dogs as Probiotic Delivery Systems*

In exploring commensuration across species in science, I realized that we have become entangled with other nonhuman species in ways that we do not fully understand at this point in time. Further, these interrelationships are playing an increasingly large role in our lives. This can easily be seen in the vast number of animal-human related posts on facebook and youtube, and the proliferation of books on animals and the animal-human bond that have been published in the past five years (Grandin and Johnson 2009; Bekoff 2007; Virga 2013; Olmert 2009). Seeking to explore this entanglement and what it may mean for both animal and human health and well-being led me to ask questions like: where do we draw the line between animals and humans, particularly when considering the myriad ways in which companion animals and humans co-create the microenvironments that live within and on the body? As we have co-evolved with

[3] In June 2015, the US Fish and Wildlife Service gave research chimps endangered-species protection, a designation only provided to wild chimps prior to this. This new protection prevents scientists from engaging or stressing chimpanzees for research unless they can show that it will have benefit for wild chimpanzees. It should be noted that some behavioral research has been allowed to continue.

companion animals, especially dogs, we have had a profound impact on the biological and social elements of one another. How then can we understand the ways in which these entanglements have impacted one another's health and well-being and how might we be able to harness these interloping effects to improve the lives of both species? These questions were pivotal in designing the "Dogs as Probiotics" study. This study looks specifically at how the introduction of a pet dog impacts the microbiome of both dogs and humans, and immunity and psycho-social well-being of humans. Further, ethnographic interviews focus on how individuals understand, interpret and incorporate ideas about microbes, microbial transfer between pet dogs and any effects this transfer might have on the human-canine relationship. Data from these interviews form the basis for the third paper in this dissertation, "Pets and the Human Microbiome, Perceptions of Dogs as Probiotic Delivery Systems."

Here I look at the ways in which individuals use pre-existing lenses through which to understand the body, animals, and human-animal/environment relationships. Although other concepts and lenses did emerge in our conversations, in this paper I explore the three most predominant lenses, namely the hygiene hypothesis, the antibiotic paradox, and dog saliva as a potential antibiotic solution and/or source of healthful bacteria. Through the use of various examples and narratives from participants who fostered a dog in the study, and interviews with individuals who contacted me from various global settings, I argue that interspecies relationships are mediated and shaped through a circulation of information available from various sources and filtered through existing lenses. These filters play an important role in the ways in which individuals think about and act on certain ideas and reveal a great deal about how people imagine health in

relation to a broadly-interpreted environment, including at the individual, interpersonal, and interspecies level. As evidenced by the emergence of the One Health Initiative, the connections between animal and human health will be taken more seriously by local, national and global health organizations (One Health Initiative 2016). Understanding the ways in which individuals interpret and utilize information about the entanglements between humans, animals, and their shared micro- and macro-environments will become critical to ensuring that programs, policies, and research are attentive to these issues.

Theoretical Lenses

The three papers in this dissertation broadly examine the ways in which the body - human, animal, and microbial – is socially constructed and produced for use in biomedical research and how individuals interact with these ideas, the biomedical research apparatus, and "evidence-based" data derived from such studies. They explore the ways in which human and other animal bodies are constructed and utilized as objects of science and knowledge production and how they are variously marked as "right," "acceptable," or "appropriate" for use in research.

In addressing these issues, I drew upon several social theories to better understand the biopolitics of clinical trials, and to conduct a posthuman ethnography of animal use in trials and how both the public and scientists view this use. The five concepts I have drawn upon most include 1) local biology, 2) biolooping, 3) commensuration, 4) the biovalue of bodies, and 5) the microbiome as space in which ideas about the body, self, and relationships to animals and the natural world, are being reimagined.

I have also drawn inspiration from Latour's early work in which he investigated the social construction of scientific objects of study in the laboratory setting (Woolgar

and Latour 1979). Although today he has reconsidered much of this writing, and it was criticized at the time for imposing the idea of a social construction on even those areas where it had no bearing, this work was pivotal in showing that scientific activity and knowledge production do not exist on their own and without the influence of those minds who are creating and interpreting them. Latour's work encouraged us to see that science itself is a culture, and is strongly influenced by the beliefs, traditions, and culturally specific practices of those who engage in it. Importantly for my work, it encourages an attention to the social ways in which scientists, doctors, the media, and lay public engage with scientific activity and are therefore entangled in the outcomes. Latour's later work on actor-network theory is also instructive, particularly in that it emphasizes an attentiveness to the role of nonhuman "actants" including pathogens, technologies, and animals in terms of how they influence their surroundings which in turn shapes material outcomes including human-human and human-animal relationships (Callon 1986; Latour 1983, 1991; 1992; 2004; 2005). Although this dissertation does not engage actor-network theory per se, it draws on this theoretical lens to show how animal, microbe, and human actants influence and co-shape one another via the process of their interactions. Rock et. al. have aptly described this process by saying: "the agency of non-human entities is not seen as being derivative of or dependent on the actions of humans, but as a constitutive part of relations that reciprocally shape both humans and non-humans" (2014: 340).

Lenses 1 and 2: Local Biology and Biolooping

Humans, animals, and the environment are all dynamic entities and profoundly impact the lives of one another, often in invisible ways. Local biology is a useful tool that can help illuminate some of this invisibility by showing how these interactions map onto the

body in ways that affect everyday health and well-being. Local biology as a term was coined by Lock in an effort to describe the interconnections and feedback loops that exist between biology, culture, and the environment (Lock 1995). She stated, "it is appropriate to think of biology and culture as in a continuous feedback relationship of ongoing exchange, in which *both* are subject to variation" (Lock and Kaufert 2001: 503, emphasis in original). Further expanding on this idea, Lock and Nguyen later defined local biologies as "the way in which biological and social processes are inseparably entangled over time, resulting in human biological difference - difference that may or may not be subjectively discernible by individuals" (2010: 90, emphasis mine). Importantly, local biology is a dynamic process that involves what Hacking (1999) has referred to as "biolooping,"which describes the interpolation of information flows between the mind, body, and environment in a continual feedback loop such that the physical experiences come to change or mediate psychological understandings and vice versa. In her more recent work on local biology, Lock (2013) has emphasized the non-linear dynamics of local biology with respect to feedback loops. Feedback loops, she now suggests, are too linear to accurately capture the complexity of the interrelationships, dynamism, and continual movement of flows of information between these entities.

The concept of local biologies is borne out of Lock's efforts to explain the differences she saw in her research on the physical and social experiences of women undergoing menopause in Japan, the US, and Canada (Lock 1995). Her research showed that Japanese women's physical and psychosocial experiences of menopause were notably different than their North American counterparts. In an effort to describe this, she hypothesized that it might in fact be due to cultural differences in the ways in which

menopause is viewed, embodied, and lived. Importantly, this included environmental factors such as diet, exercise, and pharmaceutical use (Lock 1995; Lock and Kaufert 2001). In the time since Lock published her study, the connections between diet and menopause, particularly diets rich in soy isoflavones, have been well studied. Some studies have suggested that diets rich in soy can help alleviate menopausal conditions and breast cancer risk particularly among Asian women, while others suggest that diets high in them could exacerbate hot flash symptoms and result in other adverse health effects for women such as increased breast cancer, especially among Western women (Dong and Qin 2011). However, the majority of these scientific studies looking at the impact of soy on menopause have considered these elements in relation only to one another and not in relation to other factors that may be intersecting and imparting important effects such as, but not limited to, diet, alcohol intake, environmental factors such as pollution levels, smoking status, contraception history, fluctuations in other hormonal levels, stress, as well as cultural ways of thinking about and/or discussing menstruation, menopause, and other aspects of female lifespan biology.[4]

Interestingly, when Melby returned to Japan nearly twenty years after Lock's research was published to explore how the experience of menopause had changed over time, she found that reports of hot flash-like symptoms had nearly doubled, as had reports of other symptoms such as increased appetite, chilliness, and stiff shoulders (Melby 2005). And while menopausal symptoms in Japanese women remained significantly below their North American counterparts, Melby suggested that the shift in

[4] When I lived and worked in Japan in the 1990s, public offices continued to allow women 3-4 days of paid leave of absence for "monthly female problems" Additionally it should be noted that many Buddhist and Shinto shrines do not allow menstruating women to enter given taboos on blood, particularly menstrual blood.

diet, lifestyle, and cultural views of menopause had become increasingly more medicalized in Japan. These shifting cultural views of menopause were coupled with dietary changes which rapidly and drastically increased women's consumption of calories, fat, sugar, meat, and dairy. Additionally, this was all happening at a period of rapid economic and social change in Japan during which more women entered the workforce than ever before and were expected to work incredibly long hours in very stressful environments. Looking at all of these factors together, Melby suggested that this change in hot flash symptoms was the result of the co-constitutive feedback loop of biology, culture, and environment at work over time. There is however, another very salient variable that Melby's account doesn't take into consideration, but which is important from the perspective of local biology and biolooping. That is - how soy is consumed over the lifespan. It is possible that early life consumption of soy (which is high in the Japanese context) could matter most in terms of how the body reacts over the lifespan, and as such is an important variable in considering how context unfolds.

Kontos (1999) applied local biology to her work on aging to examine how the body searches for meaning and in an effort to describe how the experience of ageing is not purely biological but rather occurs through the body and is shaped via the context of lived experience. In contrast to other social scientists who focus on the dominance of either culture or the social over the biological (Myerhoff 1992; Butler 1993), Kontos shows how the experience of aging is shaped by both the cultural and physical environments for a group of elderly in home-based care (Kontos 1998; 1999). She concludes that the experience of aging cannot be reduced to a universally experienced set of biological or physiological processes because they are in constant

interaction with the physical and social surroundings. She aptly notes that local biology "provides a conception of the body as a material phenomenon without eliding its materiality with a fixed biological essence…it provides a way of problematizing and rethinking the relations between biology, culture, and place by showing not their fundamental identity or reducibility, but the torsion of one into the other" (1999: 687).

Recently, anthropologists have worked to expand further upon Lock's definition of local biologies in ways that have endeavored to show that biology is both a place where difference registers and ethnography is crucial to understanding how it shapes and is shaped by the social (Brotherton and Nguyen 2013). This dissertation follows in this vein, expanding the use and boundaries of local biologies to include not just the human but also the non-human animal and microbial worlds, which have, with the exception of zoonoses, been largely excluded from this literature.

In the "Politics of Local Biology" I explore the ways through which biology, culture, history, environment – both macro and micro, and politics become entangled with one another. This entanglement has been used in the development of an entire sub-industry of clinical research studies whose goal it is to determine whether foreign developed drugs are safe to be used on Japanese populations. It is in this process of entanglement of all of these factors that we see truly how difference registers both at the site of the body and more globally, and how this can be taken up by global institutions in ways that profoundly impact drug development, use, and regulation.

Although local biology is not a lens that I use in the second paper, "Flexible (In)commensurabilities," it is indexed as a concern and expressed by several scientists interviewed, who noted that data from laboratory animals may be impacted by the

environments in which these animals are held. As such, environments in which lab animals are housed could be causing these animals to look much different than other animals not held in captivity. Scientists have recently started exploring this issue and are now acknowledging that it could be profoundly impacting study data and its ability to translate into humans (Martin 2010).

The last paper in this dissertation trilogy, "Pets and the Human Microbiome," extends the notion of local biology into both the animal and microbial in order to explore the ways in which they play roles in the construction of what is both "human" and "the body" in science. This paper is a unique contribution to the emerging field of multi-species ethnography in anthropology as it examines the ways in which humans, animals, and microbes intersect, interact, and influence one another. Although science has long understood the negative implications of microbes and zoonoses for human health (World Health Organization 2016), recently scientific data begun to suggest how they are both potentially positive influences on human health and well-being (Hodgson and Darling 2011). While this paper does not examine the tangible biological ways in which these beings do or do not impact one another (these data will be explored in subsequent publications), it offers a unique opportunity to see how humans use microbes in order to think and talk about, understand, and navigate their relationship with animal health and disease. Importantly, animals, and in particular pet dogs, also offer a space for individuals to begin to rethink their understandings of and relationships with various nonhuman entities.

Moreover, all three papers in this dissertation show the importance and power that ethnography brings to examinations of local biology because taking biology

seriously requires paying attention to lived and embodied experiences of individuals (Brotherton and Nguyen 2013). As Lock pointed out in her paper revisiting the topic of the nature / nurture divide in relation to the epigenome, we are moving into an era of scientific research and discovery that relies more heavily on reductionism than ever before (Lock 2013). As such, ethnography will become even more important in order to contextualize the ways in which biology and the body are enmeshed in the social aspects of everyday life. Further, Lock notes that ethnographies of local biology can help us move medical anthropology into new examinations of biomedicine. This is because while medical anthropologists have worked hard to incorporate those factors that underlie poor health including social inequalities and injustice into our work, we have largely failed to critically examine the way in which the body is made into an object of study in biomedicine. As the starting point for all studies of health and disease, this requires further interrogation.

> "One result of disembodying anthropological subjects has been the 'body proper' – the body that has enabled singular advances in the biosciences – has been left largely untroubled by thoughtful critique…The intent in addressing the truth-claims of biomedicine is not to demonize the standardized 'universal' body (an entity that is indispensable to medical practice today), but rather to do two things simultaneously. The first is to contextualize and embed bodies in time and space, thus destabilizing that which is assumed to be essentially universal, 'natural,' and readily standardizable, and bringing to the fore inextricable entanglements among history, the social/political, and the material. The second is to document the tensions and actual effects brought about in specific local settings when a standardized biomedicine is made use of for purposes of research and medical care" (Lock 2013: 296).

Thus, using the lens of local biology, these papers begin to challenge and unmoor the traditional views of bodies as universal, neatly commensurable for one

another, and reducible to parts that can be examined without consideration for their larger co-constitutive systems, both biological and physiological, as well as their social, historical, political, and environmental ones. This work is important as it helps to illuminate the ways in which entanglements of the biological, social, cultural, historical, political, and environmental come to be embedded in and taken up by science as "the body" and thus shapes the way the body is variously engaged with as an object of inquiry, study, and treatment in biomedicine.

Lens 3: Commensuration

Commensuration, a key concept in constructing biomedical research subjects, is directly antithetical to local biology in that it aims to flatten all of the texture that local biology seeks to make visible. Commensuration has been defined as the social process that enables "the transformation of different qualities into a common metric" (Espeland and Stevens 1998: 314). The concept is widely used in a variety of disciplines to describe the ways in which society constructs, ranks, compares and contrasts, and assigns value to various entities. Stated quite simply: "commensuration is crucial to how we categorize and make sense of the world" (Espeland and Stevens 1998: 314).

Biomedical research, whereby drugs and devices are tested in a group of human subjects in order to determine whether they are safe and/or effective to be marketed to the general population, rely on research subjects who are void of as much difference as possible in terms of their biological and physiological make-up. In short, biomedical experiments are reliant upon finding subjects that so closely resemble one another that any anomalies in the research can thusly be attributed to the drug or device itself and not differences within individuals. Difference within and between individuals in clinical trials

is considered by scientists to be "noise," or confounding agents, which can skew study results and bring data into question. Further, because commensuration works to ensure that research subjects are not only internally as similar to one another as possible but also that they are representative of the general public overall, it is believed that research results from adequately commensurate study populations can be assumed to be applicable to the "standard human" in the general population (Epstein 2007). The use of commensuration in biomedical research has thus further been defined by Lock and Nguyen, specifically in relation to its use in biomedical research studies as that which

> "allows people to be sorted into standardized groups and populations because their biology is assumed to be the same. This provides the grounds for meaningful comparisons to be made among them. Comparing apples from different orchards generates a more precise form of knowledge – about orchards, soils, farmers, or varieties – than say, comparing apples and oranges. Such comparisons are the basis of modern, scientific biomedicine" (2010: 176).

While Lock and Nguyen note that scientists are aiming to compare apples from different orchards, it is important to point out that in an effort to eliminate as much "noise" as possible, it often feels as though apples are not selected from different orchards at all, but from the same ones. This is because in the search for the most standard individuals, there is little room or tolerance for any variation. This collapse of categories, which has historically tended most often to "conceptualize sex/gender, race/ethnicity, and age as analogous or commensurate from a policy standpoint" (Epstein 20073: 143), has led to the majority of drug testing being conducted on young, white, male populations and excluding any variation (read noise) that women, various ethnic groups, individuals of various ages and those from myriad socio-political backgrounds

would bring to the mix. While activist groups worked to change this in the 1990s and biomedical research is now more inclusive of a variety of individuals than it ever has been in the past (Epstein 2007), the goal of collapsing individual characteristics and variance into a common metric that can be measured, assessed, and interpreted continues to be one of the primary considerations in recruiting for biomedical research studies.

Clinical research continues to ignore these various factors, despite a plethora of research that has shown the ways in which biosocial factors contribute negatively (or positively) to the health and well-being of individuals and populations over the life-course (Gravlee 2009; Krieger and Smith 2004; Krieger 2003; Hertzman and Boyce 2010; Lupien et al. 2001; Pike 2005; McEwen 2003; McDade 2002). Biosocial factors, especially local biologies, are largely ignored and/or statistically tuned out in clinical trials. As Lock and Nguyen state:

> "The reality of human difference is a fundamental challenge to the interpretation of findings of these natural experiments. Are the phenomena observed in certain people due to the specific factors under study, or might they be due to biological differences among the involved people? To combat this difficulty, large numbers of subjects are included in the study and geographic, social, and even 'racial' diversity is ensured. Large numbers allow statistical calculations to prune out the 'noise' of human variation, establish a 'quantitative average,' and hence the biological norm it is assumed to represent" (2010:181).

So while commensurability allows human biological diversity to be largely collapsed in clinical research studies, another variable of these studies, randomization, is used to ensure that any biological variation that *does* exist between individuals in the study population is equally distributed throughout all arms of the study and any differences seen can be attributed to chance (Lock and Nguyen 2010: 183). Thus, randomization and

commensurability taken together provide researchers confidence that their findings can be considered to be based on the average individual in the study population, and thusly representative and able to be extrapolated to the average individual in the general population. However, average patients in a study are just that – *the average of the study population* - not the average of the whole population. Just because randomization is said to "control" for and explain away differences between individuals "inside" a clinical trial, does not mean that it accounts for differences between an RCT study population and the general population "outside" of it (Lock and Nguyen 2010:188). Therefore, although the elements of a clinical trial, and in particular commensurability, help to ensure greater study internal validity eliminating as many confounding factors as possible, it actually negatively impacts the "external validity" or generalizability of the study to the general public. Quite simply, the greater the internal validity of a study, the less its external validity (Lock and Nguyen 2010).[5] The more rigorous and homogenous a study population, made so by commensuration, the less likely it is that it will resemble a "real world" population (Lock and Nguyen 2010; Lewith et. al. 2011).[6]

Increasing the internal validity through the elimination of factors considered to be confounders or noise allows researchers to determine that any differences observed in the study can accurately be attributed to the "specific effects" of the therapy under study

[5] It is important to note here that internal validity in a study can take many forms. What I argue for, and what other social scientists have as well (Lock and Nguyen 2010; Epstein 2007), is greater inclusion of techniques to increase internal validity that incorporate the biosocial aspects of human life.

[6] This is in fact a large part of the reason why Phase IV, or post-marketing studies of drugs exist. Once a drug is approved by the Food and Drug Administration (FDA) and made available to the general public, physicians are at liberty to prescribe it to people who will, almost surely, bear very little resemblance to the populations originally used to test the drug. Individuals will have various comorbidities, be taking any number of drugs and/or supplements, as well as have varied socio-economic, lifestyle, and environmental factors in their lives that can greatly impact the effect of a drug on their bodies. The first ten years following a drug's approval is considered to be the post-marketing surveillance period during which physicians, drug companies, and regulatory agencies encourage consumers and patients to report any adverse and/or positive side effects of the drug to their doctors and / or regulatory bodies.

(IOM 2005). However, critics of evidence based medicine (EBM) and practitioners / researchers of complementary and alternative medicine have long suggested that these very aspects considered noise in clinical trials (i.e. nonspecific effects) may actually play an important role in the effectiveness of both complementary and alternative medicine (CAM) and biomedicine (Kirsch 1997; IOM 2005; Thompson, Ritenbaugh, and Nichter 2009). Much of the way health and illness are approached in CAM modalities is predicated on the idea of difference between individuals that will affect the ways in which they respond to both the specific and nonspecific effects of therapy. And as stated above, biosocial factors also play an important role in how individuals respond to medical treatment. As such, collapsing individuals down into a few common metrics in order that a treatment's effects might be able to be more clearly seen is problematic not only because of the variance between these individuals, but also because it also allows for an erasure of those specific, individualized aspects of any given person that will have a profound impact on his/her response to a medication.

Thus, in this dissertation which broadly examines the body as a constructed object in biomedicine, the social processes by which commensuration is enacted serves as a powerful tool through which to examine not only how bodies are made to be similar to one another, but also how, via political and historical forces, they might be made to be dissimilar in the same moment. This is the case in both papers that use commensuration as a lens: "The Politics of Local Biology" and "Flexible (In)Commensurabilities." In examining the ethno-bridging clinical study apparatus that the Japanese regulatory authorities have insisted that all foreign drugs must go through before they can be marketed in Japan, I explore the biopolitical forces that have shaped the development of

this field. Ethno-bridging studies are predicated on the idea that Japanese bodies are different from all other human bodies in very real, discernable, and tangible ways that have important implications in the development of drugs that will be ingested by these unique bodies. While other nations generally accept data collected from one geographic region to support the application of a drug for marketing, Japan insists that inherent characteristics in the Japanese require these drugs to be retested specifically on populations of Japanese people and submission of this data for approval to Japanese regulatory authorities to review. It is in this overtly biopolitical act that renders Japanese people as uniquely distinct in their brains and bodies from others, that the Japanese wholly refute the idea that characteristics shared between human bodies can be collapsed into categories that make them measurable in the same way. Ethnobridging studies, by virtue of their very existence, are resolutely making a statement against the social processes of commensuration in the biomedical research project. This paper also closely examines the ways in which local biology and social processes are integral to clinical trials and why, even though they attempt to incorporate these factors, ethno-bridging studies still fail to fully incorporate these concepts into the study of drug trials for the Japanese market.

In "Flexible (In)Commensurabilities" I extend my examination of the social process of commensuration in biomedical research studies to pre-clinical research studies where non-human animals are used as research subjects to determine whether a drug is safe enough to be tested on a human population. Animals have played an important role in the drug development process, and likely will for many years to come. They are the first set of subjects on which drugs are tested in order to determine whether their

pharmacodynamic and pharmacokinetic profiles are safe enough to move the drugs into humans. Mice are most often used as the first line of testing, and then if found to be safe in this model, a second animal model is selected. Selection of this model is usually based on the similarity between the animal and human organ or system that the drug is targeting. For example, ferrets are often used for respiratory drugs, canines for cardiac drugs, and so forth. However, given that an entire industry has been developed to test the extent to which differences between Japanese and non-Japanese individuals matter in terms of a drug's effect in the body, it seemed important and informative to extend this examination to the ways in which species differences between nonhuman and human animals do (or do not) play a role in the drug development process. Paper 2 paper explores the ways in which scientists construct NHPs as simultaneously (in)commensurate for humans and how this process co-creates our views of animals and our views of ourselves as human animals. It also discusses potential implications for science and society of the ways in which animals are rendered similar but different.

Lens Four: Biovalue

Valuation is a key component in rendering objects commensurate or incommensurate for one another. Social scientists of medicine have been describing the ways in which bodies are commodified and valued in the biomedical sciences for some time now. This valuation of bodies has been termed "biovalue." Waldby and Mitchell coined this term and defines biovalue as "vitality and profitability produced by the biotechnical reformulation of living processes" (2006: 336). Her their, which focuses on tissue banks, originally used this term to describe the ways in which tissues from the dead are reformulated and then used to enhance the vitality and health, and preserve the lives

of, the living (Waldby and Mitchell 2006; Mitchell and Waldby 2010). However, social scientists have expanded on the notion of biovalue to include those processes of valuation that are enacted upon living bodies. As such, they have variously used biovalue in order to describe the ways in which individuals, biotech corporations, governments, and pharmaceutical companies are engaged in the use and reformulation of blood, human tissues, organs, cells, and the body itself in ways that are then able to be assigned a value through the process of commodification, and marketed, sold or exchanged in the neo-liberal market place (Scheper-Hughes 2002; Sunder Rajan 2006; Triendl and Gottweis 2008; Wahlberg 2009; Mitchell and Waldby 2010). Others have specifically described the ways in which human bodies are assigned biovalues and thus utilized in the transnational pharmaceutical market in ways that benefit pharma, governments, and individuals but can also be significantly problematic, especially for those whose bodies are being utilized in these ways (Sunder Rajan 2006; Petryna 2008).

Rose and Novas (2005) have described the economically productive value of life as one important dimension of biovalue. Importantly, it relates closely to commensuration and the construction of bodies such that they can be used in the process of creating capital. They note how the system of biomedicine, in its construction of bodies that can be rendered usable in the scientific apparatus, imbues them with a value that can then be capitalized on by individuals, governments, corporations, activists and so on.

> "Contemporary biomedicine, by rendering the depths of the body visible, intelligible, calculable, and capable of intervention at a molecular level, makes it amenable to the production of economic value. In many ways, what is being accomplished through the life science is a kind of "flattening' of the vital processes of the body. This not only

> enables these 'surfaces' to become equivalent with one another at the most basic biological level, but also allows them to be enfolded within the processes of capital or social accumulation. They contain the potential to transform each and every one of us into a standing reserve for the creation of biovalue" (2005: 455).

Commensuration "flattens" the body into characteristics that allow only those very basic biological processes to be considered pivotal. Analysis based on these characteristics alone is then used to create marketable drugs. And because this process uses only certain characteristics from certain bodies, it places bodies in a hierarchy where the biovalue of some is greater than others. As noted, historically this has meant that young, white, male bodies were more valued than others (Epstein 2007), but in today's globalized pharmaceutical world in which genomics and individualized medicine is a growing sector of the market, niche standardization is driving the push to increase diversity in clinical trials. This has increased the offshoring of studies to places like India and Brazil where cultural, racial, and ethnic diversity can be easily obtained in these racially diverse nations (Sunder Rajan 2006; Petryna 2008). The papers in this dissertation also deal with the issue of valuation of certain bodies over others in the drug development market, and the ways in which biovalue is assigned to various bodies and what this means for those living in those bodies, those enacting scientific experiments upon them, and ultimately the meanings that this has for the science itself.

In "Politics of Local Biology" I describe how biovalue of Japanese bodies has various meaning and importance for those Japanese citizens who take part in ethno-bridging studies. The government is undertaking a biopolitical project in its creation of a unique 'Japanese bioidentity' and both the government and individuals are shaping this identity through the enrollment of such bodies in ethnobridging studies. For

pharmaceutical companies hoping to gain access to the Japanese market, Japanese bodies are imbued with a biovalue that in turn provides access to markets and profits that are obtained through the use of these bodies in the scientific process. In "Flexible (In)Commensurabilities" I examine the ways in which the process of constructing NHP bodies for use as proxies for human bodies in scientific research renders some NHPs as so similar to humans that their biovalue is considered too high to be used as research subjects. On the flip side of this, however, is the process whereby other NHPs, namely non-apes, are considered to be similar to humans such that they can be used as proxies for humans in research, but because they are not like humans in the important social and emotional ways they are viewed as incommensurate with humans, assigned a lower value than their ape counterparts, and thus able to be used in biomedical experiments. Similar to how biovalue is described by Rose and Novas above, when used in scientific research studies as proxies for humans, animal bodies are flattened into those characteristics that most resemble humans, and which allow them "to become equivalent with one another at the most basic biological level" (Rose and Novas 2005: 445). These are then used to generate data, knowledge, and profits for those engaged in the scientific economy of biomedical research. Animals become commodities with biovalues that are often different for each group involved in the research: scientists, pharmaceutical companies, diseased individuals, the government and regulatory authorities, and pro/anti animal rights activists. This paper thus extends biovalue from Waldby and Mitchell's (2006) original intent to describe how matter from deceased human beings can bring vitality, life, and profitability to the living, to how animals' biovalues become an integral component of the construction of bodies and scientific knowledge.

Lens Five: Microbiome

As we consider the value that other species have in terms of scientific advances for human health and well-being, biomedical researchers and social scientists have begun to look more closely at the role of another species in this regard, that of microbes and the human microbiota. In fact, one of the most notable scientific discoveries of the last decade has been the important roles that the trillions of micro-organisms in our guts and saliva, and on our skin and internal organs, that are commonly known as the microbiota, play in promoting good physical health and emotional well-being. Scientific research on the microbiota has exploded in recent years, and this has changed the ways that scientists, doctors, lay publics, and social scientists now think about microbes. What were once mostly thought of as vectors of disease, allergens, and pathogens are now known to have important and potentially life-altering health promoting and life-giving properties. Data from pre-clinical studies to date suggests that the microbiome plays a mediating role in several key biological and physiological functions including autoimmunity (Horai et. al. 2015), cognition (Gareau 2014; Smith et.al. 2014), the blood-brain barrier function (Braniste et. al. 2014;), systemic inflammation (Forsythe 2007; Karimi et. al. 2009; Minniello et. al. 2010; Forsberg et. al. 2013; Belkaid and Segre 2014) and neuroinflammation (Lee et. al. 2011), emotional behavior (Bravo et. al. 2011; Smith et. al. 2014; Heijtza 2011), and mental health and psychiatric illnesses (Rook et.al. 2014; Haroon et. al. 2012; Miller and Raison 2015; Raison et. al. 2010; Rook et. al. 2013; Rook et. al. 2014). Other population based studies support these findings, suggesting that children raised in homes and environments where they are exposed to dirt and pathogens at an early age do not develop autoimmune disorders and asthma at the rates that those

raised in more "clean" or microbe deficient environments do (Yazdanbakhsh et. al. 2002; Almqvist et. al. 2003; Havstad et. al. 2011; Hanski et. al. 2012; Lynch et. al. 2014).

It has been suggested that one very important factor that damages the microbiota in the modern world is our separation from many micro-organisms with which we co-evolved (Rook 2010). These micro-organisms have the ability to lower the types of chronic inflammation that are ubiquitous in the modern world and that contribute to the development of most of our most pressing health issues, from diabetes and heart disease to depression and dementia (Raison et. al. 2010). These findings support the "hygiene hypothesis" first introduced in 1989 which suggests that the spike in allergic diseases in Western countries is largely the artifact of hyper-clean and relatively pathogen-free environments that modern humans inhabit in Western societies (Strachan 1989). This hypothesis has been expanded in recent years and has come to be known as the "old friends" mechanism (Rook et. al. 2010; 2014). "Old Friends" has broadened this concept such that it is now a fundamental aspect of evolutionary medicine and is integral to thinking about and understanding the breadth of interactions between human and animals and their environments (Rook et.al. 2014). Importantly, microbiota play a key role in the old friends mechanism, particularly in regards to the feedback loops that exist between these organisms, the various physiologic systems of the body in which they live, the brain, and the larger environment, both natural and built (Rook et.al. 2014; Hoisington et. al. 2015).

Anthropologists have in recent years begun to take up the issue of the microbiome and are poised to contribute in unique and important ways from biological and evolutionary perspectives (Kirksey and Helmreich 2010; Benezra et. al. 2012; Warinner

and Lewis 2015). Some of the important ways in which anthropologists are contributing to this field to date include the etiology and treatment for tuberculosis (Inhorn and Brown 1990; Farmer 1997; Koch 2013), human diet (De Filippo and Tuohy 2015), human migration (Dominguez and Martin 2011), gene-culture (Laland et. al. 2010; Disotell 2003), the ways in which social ties and kinship interact in human microbial communities (Carsten 2000); lifecourse biology and changes in the microbiota over time (McDade et. al. 2010), and the ways in which socio-economic status and gender impact the microbiota (Ravel et. al. 2011). Additionally, investigations into what an "indigenous" or "original" human microbe can tell us about our own evolution as a species and co-evolution with other species is underway (Bankoff et. al. 2015), as is research into how these data can inform our understandings of human and animal health and disease (Warriner and Lewis 2015; Laland 2010; Disotell 2003). In turn, these findings could play an important role in the development of treatments in both human and veterinary medicine.

And yet despite anthropology's attention to the microbiota on this host of issues in relation to the microbiome, there remains a dearth of research being conducted in two key areas as they relate to the interloping and feedback loops in human health and disease, namely animals and the environment. Hoisington et. al. (2015) have suggested that the microbiome of the built environment (MoBE) in Western societies may be a key way in which disease-causing microbes, particularly those implicated in neuropsychiatric disorders, are spread among humans. They call for further research into the microbiology of psychiatric disorders as well as microbiological and anthropological investigations of built environments to better understand the interconnections between the environment, microbes, and disease transmission. While multi-species research and ethnographies are

on the rise in the social sciences in recent years (Kirksey and Helmreich 2010; Haraway 2003; 2008), and much has been written about the positive psychosocial impacts that animal-human relationships have on human psychological health (for a review of this literature see Wells 2007), there remains little investigation into the social aspects of the animal-human-microbe nexus. To date, most medical anthropological and public health research on the intersectionality of animals and humans primarily focuses on zoonotic diseases, risks to humans, and control (Green 2012, Hinchliffe et al. 2012). More recently, there has been a growing interest in gut and immune system evolutionary advantages of close animal-human relationship (Song et. al. 2013; Almqvist 2003). Work in this dissertation aims to contribute to this growing field by expanding on these areas.

As noted above, because the health of the microbiome (animal, human, and environmental) is closely tied to diet, migration, history, socio-economic status, life-course biology, evolution, culture, and genes, it offers the perfect opportunity for anthropologists to further expand upon and apply the idea of local biology and biolooping/feedback mechanisms. As such, the third project that composes this dissertation is an attempt to explore this aspect of local biology, namely the role that animals, particularly pet dogs, play in improving (or not) the microbiota of elderly individuals. Additionally this study is looking at what, if any effect a change in the microbiota may have on immune function and psycho-social well-being, or how these variables may be independently interacting and modifying functions of the body and brain. Although the paper that discusses this study focuses primarily on the ways in which participants make sense of the microbiome, it offers useful insights into how individuals are thinking about these issues and interpreting the ways in which their

interactions with the world around them impacts their health. As an anthropologist, I insisted that qualitative and ethnographic research methods be included in the study design in order that any changes seen in the biomarkers could be triangulated with additional data, and a more robust picture of individuals' experiences could emerge. As noted above in relation to local biology, ethnography also plays an important role in understanding the microbiome in terms of its role in human ecology and multispecies relationships.

Methods and Sampling

Each paper is written using data from one part of a larger project on that topical area. These three separate projects on construction of bodies in Japanese ethnobridging studies, the use of NHPs in biomedical research as proxies for humans, and the potential of pet dogs to serve as probiotics for human owners, together comprise the overarching program of research I conducted as a graduate student at the University of Arizona. I employed several ethnographic methods in each of the three projects in order to facilitate data triangulation and to ensure that the multiple stakeholder voices important to each of these topical areas were engaged. Table 1 (below) specifies the methods and sampling used in each of the projects. Specific methods and sampling used in each of the papers is described in greater detail in the following chapters.

TABLE 1: Dissertation Project Methods

Specific Ethnographic Methods Used	Specific Study in Which the Ethnographic Methods Were Employed			Sampling
	Japanese Ethnobridging Study	Nonhuman Primates in Biomedical Research	Dogs as Probiotics	
Literature Review	X*	X	X	NA
Archival Research	X	X		NA
Review and analysis of clinical trial recruitment websites	X			Japanese Ethnobridge: N= 30*
Review of letters, notes, and writings done while living abroad**	X			NA
Participant Observation		X	X	NHP: Two sessions were conducted at each zoo.^ Dogs as Probiotics: Weekly observations conducted at the Humane Society, training sessions at homes and dog parks, and in participants homes.^^
Key informant interviews	X	X	X	Japanese Ethnobridge: N= 2 NHP: N= 5 Dogs as Probiotics: N= 5
Semi-structured in-depth interviews	X	X	X	Japanese Ethnobridge: N= 10 NHP: - Scientists = 22 - Lay persons = 35 - Activists = 5 - Veterinarians = 2 Dogs as Probiotics: N = 27
Life history narratives		X	X	NHP: - Scientists = 20 - Lay persons = 35 - Activists = 5 - Veterinarians = 2
Analysis of emails written to me following media coverage and used for data analysis			X	Dogs as Probiotics: N = 54

Table 1, Dissertation Methods Continued

Free association exercises		X		NHP: - Lay persons = 35
Card sorting activities		X		NHP: - Lay persons = 20
Analysis of comments on on-line news articles and forums*	X	X	X	NA
Analysis of informational, activist, and professional websites		X		N= 10
Buccal, skin, and fecal swabs for microbiota analysis			X	Humans = 17@5x Canines = 14@5x
Blood collection for analysis of immune changes			X	Humans = 17@4x
Psycho-social questionnaires to assess loneliness, depression, quality of life**			X	Humans = 17@4x
Heart rate variability testing			X	Humans = 17@4x
In depth dietary analysis using 24-Hour Recall			X	Humans = 17@4x
Activity assessment using Actigraph			X	Humans = 17@4x

* Both English and Japanese sources

** I lived in Japan for several years prior to beginning this research, however, during those years I wrote a great number of letters and emails to family and friends. I also kept diaries and logs of my experiences, many of which dealt with my experiences around the embodiment of being different as a gaijin and the perpetual stigma associated with being an outsider.

α Participant observation conducted at the San Diego, Milwaukee, Phoenix, and Tucson Zoos in the United States

α, α Participant observation conducted Humane Society of Southern Arizona and in participants' homes, dog parks, and dog training sessions

*Facebook was not used because their privacy regulations and guidelines prohibit the use of comments from Facebook unless the researcher specifically receives informed consent from the person making the comment.

** Specific questionnaires included: Quality of Life, Enjoyment and Satisfaction (Q-LES); WHO-5; Inventory of Depressive Symptomatology (Self Report) IDS-SR; the Short Form-36;UCLA Loneliness Scale; Mini-Cognition Test; International Physical Activity Questionnaire (IPAQ) ; Lexington Attachment to Pets; Proximity to Pets questionnaire; Dogs and Physical Activity Tool (DAPA); Schneider QoL Scale for the Dog

Conclusion

Science and scientific knowledge production do not exist in a vacuum, but rather are very heavily influenced by and are a product of the society that constructs it. The social world in which it circulates, its cultural aspects, and those who construct it – scientists, medical professionals, the media and lay persons - are as much a part of science as the science itself. Therefore, understanding the ways in which the body – the central focus of biomedical research – is biosocially constructed as *the* object of study, is paramount to understanding science and medicine. Moreover, an interrogation of the methods used to construct bodies – human, animal, and microbial - as objects of science, provide opportunities to understand how these techniques may at times be problematic and working in counter-intuitive ways. It also provides an opening to better understand the ways in which individuals understand, interpret, and utilize scientific knowledge in their daily lives and how this impacts the biosocial ways in which we live. This dissertation has examined the social construction of the body in science using one example each from the world of human, animal, and multispecies clinical trials. Through an exploration of the issues in each of these cases, I show that these constructions and the ways in which they are negotiated, contested, and taken up in daily life are flexible, malleable, and not at all uniform. They are messy and at times in conflict with one another, and there are rarely clear black and white lines. This is exactly why it is so important to interrogate how the very essence of biomedical knowledge – the body – is socially constructed and how it co-creates the animal, microbial, environmental, and cultural worlds in which it circulates. Through doing so and using techniques and lenses

grounded in biosocial anthropology, this dissertation adds to the literature on the body in both medical and multispecies anthropology.

CHAPTER 1

The Politics of Local Biology in Transnational Drug Testing: Creating (Bio)Identities and Reproducing (Bio)Nationalism through Japanese "Ethnobridging" Studies

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Introduction

Next to the United States (US), Japan is the second largest pharmaceutical market in the world in terms of expenditures (Iseki 2001). Although Japan's population is only 2% of the world's population (Statistics Bureau 2010), it represents 12% of global pharmaceutical sales (Sands 2001), and at a 10% growth rate, has outpaced both the markets of the United States and those of the European Union (EU) (Bentley 1997). Notably, the presence of western drugs (defined here as those developed and marketed by companies in the USA and the EU) in the Japanese market is incredibly low (Jhee et. al. 2006). Only 40% of the drugs approved in the US have been approved in Japan (Sands 2001). Reasons for this include the long time it takes for New Chemical Entities (NCEs) to receive approval for testing and the lengthy clinical trial period required by the Japanese Ministry of Health, Labor, and Welfare (MHLW). In 1998, the US, EU, and Japan all adopted the "ICH Efficacy Topic E5", which are a set of guidelines that enable clinical trial data generated in one member region to be used in another for the purposes of regulatory approval, a practice known as bridging. (Ruckle 2009). While these guidelines cover bridging studies in general, they primarily provide provisions for "Ethnic Factors in the Acceptability of Foreign Clinical Data" which recognizes that in some cases drug trials are called for to test the action of drugs in specific ethnic groups due to the unique characteristics of these groups (Ruckle 2009). While this policy agreement did help to decrease the amount of time it takes some Western drugs to enter the Japanese market, requirements by the MHLW for the approval of Western drugs now almost *always* require the inclusion of additional "ethno-bridging" studies as part of

Japan's procedures for regulatory approval. "Ethno-bridging" studies (EB studies) refer to those clinical trials that must be conducted within a target population deemed to be representative of the population for whom the drug is intended in order to collect data on the pharmacokinetics (PK), pharmacodynamics (PD), dosage, safety, and efficacy of the drug. Stated quite simply, this means that in order for a drug to be used by and on certain types of bodies, its safety and efficacy must have been already established on a group of bodies that are considered similar to those for whom the drug is intended.

A cursory consideration might lead one to make the argument that EB studies primarily serve a political economic agenda, protecting Japanese pharmaceutical interests, and providing a rationale for a protectionist doctrine. While there is some truth to this, we suggest that EB studies actually have far deeper social and cultural meanings, meanings that are tied to uniquely Japanese projects of governmentality[7] and nationalism. EB studies, we argue, accomplish three things in Japan. First, they advance the role of the government in the transnational pharmaceutical market through the protection of indigenous pharmaceutical companies. Second, they (re)define what it means to be Japanese. And third, they provide an opportunity for those who have "the correct" Japanese (bio)identity but who live outside the country, to contribute to a type of biocitizenship project (Rose and Novas 2005), which aims to both shape and exploit what it means to be biologically, ethnically, or racially "Japanese". This biocitizenship project bestows upon these expatriates and emigrants a sense of moral identity. By volunteering

[7] The concept of governmentality comes from Foucault's idea that power is a diffuse entity circulating throughout all levels of society. Governmentality, concerned with the 'art of government', describes the ways in which a wide array of actors, not just state governments, engage in activities aimed at controlling their own or others' actions. Political theorist Mitchell Dean notes that governmentality is the 'conduct of conduct', where conduct means to 'lead, direct or to guide, or implies some sort of calculation as to how this is to be done' (Dean 1999: 10).

to participate in trials that serve a national good, they reproduce and preserve a national heritage of what it means to be "Japanese".

Key to our argument is the way "ethnic-factors" are defined and operationalized in the ICH E5, and the manner in which they have become a proxy for a distinctly Japanese notion of "local biology", the idea that biological and social processes are engaged in a dynamic feedback loop (Lock and Kaufert 2001; Lock and Nguyen 2010), through which governmentality and nationalism projects are enacted. We examine how Japanese Big Pharma and government exercise biopower[8] (Dreyfus and Rabinow, 1983; Foucault 1990; Gastaldo 1997), and engage in projects of (bio)nationalism, which aim to strengthen the state through a recognition and appropriation of the biological and cultural heritage of its population (Wahlberg, 2009), through pharmaceutical policies that index a uniquely Japanese (bio)identity.

International Conference on Harmonization: Ethnic Factors in the Acceptability of Foreign Clinical Data (ICH E5) and "Ethno-bridging" Studies

While the importance of independent evaluation of drugs and devices has long been recognized and implemented by many national governments, it wasn't until the late 1980s that harmonization of national and regional regulations was deemed necessary as a way to keep pace with an increasingly global pharmaceutical marketplace (Ruckle 2009). Shortly after the European Community, (now the EU) moved toward harmonization for that region, the US, EU, and Japan began discussions on harmonization between these three regions. A harmonization agreement was eventually enacted in 1990 (Ruckle 2009).

[8] Biopower is a term coined by Foucault, which "refers to the mechanisms employed to manage the population and discipline individuals. In Foucault's view, biological life is a political event: population reproduction and disease are central to economic processes and are therefore subject to political control" (Gastaldo, 1997). We use the term biopower here to refer to the ways in which the Japanese state and Big Pharma are engaged in knowledge creation around drugs suitable for the Japanese population.

Harmonization between these three regions primarily focused on ethical and scientific parameters of clinical trials, such as the use of study designs (like the randomized, placebo-controlled clinical trial), and standardization of requirements for human subjects protections (Anonymous reviewer #1, personal communication 10/8/10).[9] Despite the usefulness of the ICH in these areas, however, foreign pharmaceutical companies continued to face high costs and lengthy timelines when trying to introduce drugs to Japan. This was because the MHLW required foreign drug companies to repeat the entire clinical drug-testing program in Japan for drugs that had already been marketed in other countries. Having to duplicate the entire investigational program in a new region was counter to the intended goals of the ICH, and in 1998, the member regions adopted the "Ethnic Factors in the Acceptability of Foreign Clinical Data Guidelines". The objectives of the ICH E5 are:

- To describe the characteristics of foreign clinical data that will facilitate their extrapolation to different populations and support their acceptance as a basis for registration of a medicine in a new region;
- To describe regulatory strategies that minimize duplication of clinical data and facilitate acceptance of foreign clinical data in the new region;
- To describe the use of bridging studies, when necessary, to allow extrapolation of foreign clinical data to a new region; and
- To describe development strategies capable of characterizing ethnic factor influences on safety, efficacy, dosage and regimen (ICH 1998:1)

A key reason for developing the ICH E5 guidelines was to create a roadmap for foreign data to be used in the clinical data packages of drugs enabling approval by the regulatory bodies of other member regions. At the same time, the language of the ICH E5 speaks to the importance of identifying "ethnic differences" which may have an impact on drug safety, efficacy, dosage, and dose regimen. Thus, we at once have guidelines to enable

[9] I have chosen to keep the names of the experts I interviewed about ethno-bridging studies anonymous in order to protect and respect their privacy.

data collected in one region to establish the safety and efficacy of a drug across regions and, simultaneously, concern registered about ethnic differences as a possible factor influencing the viability of particular drugs for particular populations. Therefore, while the ICH E5 provides a *guideline* for clinical development of drugs for the Japanese market, it is important to note that approval is granted on a case-by-case basis and differs for each drug depending on the drug's class, data that has been collected in previous studies and so forth. The ICH E5 "seeks to recommend when safety and efficacy requirements may be satisfied with foreign clinical data" but also when "additional studies conducted in any region may be required by the new region to complete the clinical data package"(ICH 1998:2).

In order to look at "ethnic differences" on drug safety, dosage, and so forth, the ICH E5 laid out a framework for data from one region to be "bridged" to a new region via studies called "ethno-bridging studies". Ethno-bridging studies are defined in the ICH E5 as studies "performed in the new region to provide pharmacodynamic or clinical data on efficacy, safety, dosage and dose regimen in the new region that will allow extrapolation of the foreign clinical data to the population in the new region" (ICH 1998:4). Upon review of ethno-bridging data, the regulatory body in the new region will determine whether or not they will require additional studies of the drug to be conducted in the new region. If additional studies are required, data from these ethno-bridging studies will be used to design the larger Phase 2 and 3 studies. Indeed, while adoption of the ICH E5 by Japan, the US, and the EU theoretically means that ethno-bridging data could suffice for MHLW approval of Western drugs for use in Japan, this rarely happens without additional full-scale studies (Phase 2 and 3) in Japan (Anonymous expert #1,

personal communication 10/8/10). In fact, a leading pioneer in this field suggests that one of the main impetuses behind the ICH E5 agreement was a push by US and EU based companies to be able to market pharmaceutical products in Japan more efficiently in terms of both time and money (Anonymous expert #1, personal communication 10/8/10). Thus, Japan's enormous potential as a market for Western drugs and the MHLW's insistence upon data from Japanese subjects before approval of drugs for the Japanese market have combined to make Japan a major focus of "ethno-bridging" studies. Prior to the ICH E5, foreign companies wishing to market drugs in Japan often were required to repeat the *entire* clinical development program (with the exception of pre-clinical testing) that had been done in the original region, a process that often took an additional decade or longer and could cost millions of dollars. (Anonymous expert #1, personal communication 10/8/10). As conversations with two leading experts in this field indicate, the issues involved in introducing Western drugs to Japan require intense negotiation with officials at the MHLW (Anonymous expert #1, personal communication 10/8/10; Anonymous expert #2, personal communication 10/11/10). These negotiations can and often do take years. Thus, the strategy of pharmaceutical firms hoping to enter the Japanese market has been to develop strong working relationships with the MHLW and to engage with them in early and frequent discussions about the development and regulatory pathways for each specific drug they plan to market in Japan. These talks almost *always* end with the MHLW making a demand for additional testing. This facilitates the development of the most appropriate clinical testing program, in which ethno-bridging studies play a key role. And, even when EB studies are required by the MHLW, it is rare that they require the entire clinical program to be replicated in Japan.

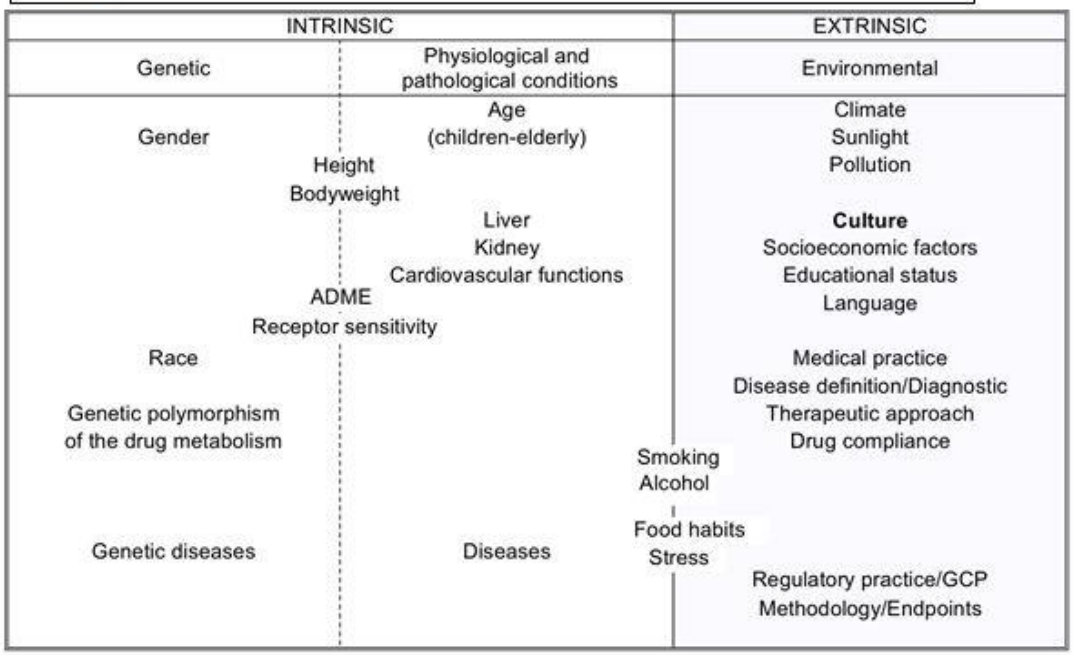
As such, even with the insistence upon ethno-bridging studies by the MHLW, the ICH E5 has meant an incredible time and cost savings for foreign pharmaceutical companies hoping to market their drugs in Japan.

As the purpose of the ICH E5 is "to facilitate the registration of medicines among ICH regions by recommending a framework for evaluating the impact of ethnic factors upon a medicine's effect," the definition of "ethnic factors" becomes critical. Ethnic factors are defined as:

> "Factors relating to races or large populations grouped according to common traits and customs. Note that this definition gives ethnicity, by virtue of its cultural as well as genetic implications, a broader meaning than racial" (ICH 1998:8).

Ethnic factors are further defined as either "intrinsic" or "extrinsic" as shown in Table 2. "Extrinsic ethnic factors" are those associated with a person's environment and culture. They are here defined as "less genetically and more culturally and behaviorally determined" and include factors such as diet, tobacco and alcohol use, exposure to pollution and sunshine, and socioeconomic status" (ICH 1998:8). "Intrinsic ethnic factors" are those, according to the ICH, that "help define and identify a subpopulation and may influence the ability to extrapolate clinical data between regions" (ICH 1998:8). Intrinsic factors include features of the physical aspects of genetics such as genetic polymorphisms, height, weight, lean body mass, body and composition, and organ dysfunction (ICH 1998:8).

Table 2: Classification of Intrinsic and Extrinsic Ethnic Factors
(ICH E5 1998: 10)



Defining these terms in this way is problematic. Note that the definition of "ethnic factors" as it is defined in the ICH E5 conflates race as ethnicity and genetics. In short it "geneticizes race" (Kahn 2006:56). However, as biological anthropologists and geneticists have long noted, "at the genetic level there is more variation between two individuals in the same population than between populations and there is no biological basis for 'race'" (Anonymous, 2001). Therefore, intra-ethnic variations at the genetic level and factors defined as "extrinsic" in the ICH E5 (diet, exercise, tobacco use, socio-economic status, etc) should be given as much attention as intrinsic factors associated with ethnic body composition or genetic differences (genetics, gender, height, body composition etc). Moreover, because these factors do not operate in vacuums, it is vitally

important for drug research to investigate the feedback and feed-forward loops that exist between these factors. However, exactly the opposite data is privileged in ethno-bridging studies, where a geneticized notion of race is valorized. Thus, as Gravlee (2009) notes in his discussion of these issues, "in lieu of explicit definitions, researchers typically use race as a proxy for some unspecified combination of environmental, behavioral, and genetic factors". Stated bluntly, the ICH's definition of "ethnic factor" serves to gloss over differences that should be important to those wanting to conduct better clinical trials. Differences and interactions between environmental, behavioral, cultural, and genetic variables are lost to a reified conception of the notion of "ethnic" bodies. In the Japanese case, a representation of an essentialized Japanese body is also underscored by a culturally robust notion of "local biology".

Local Biology: The Missing Factor in Ethno-bridging Studies

We turn now to a closer examination of the Japanese concept of "local biology" and how it has informed ethno-bridging studies and Japanese biopolitics. Lock and Nguyen define the concept of "local biologies" as referring "to the way in which *biological and social processes are inseparably entangled* over time, resulting in human biological difference — difference that may or may not be subjectively discernible by individuals (Lock and Nguyen 2010:90, emphasis mine). Lock earlier had noted "it is appropriate to think of biology and culture as in a continuous feedback relationship of ongoing exchange, in which *both* are subject to variation (Lock and Kaufert 2001 emphasis in original). "Local biology" then, is dynamic and involves what Hacking (1999) has referred to as "biolooping". "Biolooping" is a way of explaining how the mind, body, and environment send information to one another in a continual feedback loop such that the

physical experiences come to change or mediate psychological understandings and vice versa (Hacking 1999). Both "local biologies" and the ICH E5's "ethnic factors" thus point toward the importance of understanding the ways in which biology and social factors can impact human biological difference. However, the manner in which the ICH E5 is operationalized misses the critical component of a *continual feedback loop* captured in Lock and Nguyen's description. This is strongly evident in Table 1, which depicts the neat compartmentalization of intrinsic and extrinsic factors found in the ICH E5. This compartmentalization is carried over in ethno-bridging studies conducted under the ICH E5; the majority of these that get reported in the literature investigates the connection between drug effects and genetic (read ethnic) factors (Jhee et al. 2006; Ruckle 2009). While there is some literature that discusses the interactions and connections between lifestyle and drug effects (see chapter 6 of Jhee et. al. 2006 for a comprehensive overview), the majority focus only on diet, especially on alcohol use, protein intake, vitamin supplements and to a lesser degree tobacco use (Jhee et al. 2006). Seldom do these ethno-bridging studies take into consideration the other lifestyle factors mentioned in Table 1, such as socioeconomic status (SES), climate, pollution, or stress. However, research conducted by biocultural anthropologists and social epidemiologists in recent years has highlighted the many ways in which these factors contribute negatively (or positively) to the health and wellbeing of individuals and populations over the life-course (Pike 2005; McEwen 2003; McDade 2002; Lupien et al. 2001; Krieger and Smith 2004; Krieger et al. 2005; Krieger 2005; Krieger 2001; Hertzman and Boyce 2010; Gravlee 2009). Such research is important not only for public health specialists but should also be considered more carefully by those in the pharmaceutical and drug-development fields.

Factors like SES and psychosocial stress can and often do play a role not only in the types of diseases and illnesses that manifest in certain populations, but also because they very often are important in a medication's effect on individuals and populations. Much of the evidence on the impact of SES on individual and population response to drugs comes from work in the field of immunization (Worthman & Kohrt, 2005). Literature in this field has shown that factors like malnutrition, severe stress, early deficits in immune development and heavy pathogen/parasite loads limit vaccine effectiveness through compromising the immune system (Glaser, 1998; Shell-Duncan, 1995; Udani, 1994; Worthman & Kohrt, 2005).

The lack of attention ethno-bridging studies typically pay to many important extrinsic factors, as well as their neglect of the complex relationships between so-called intrinsic and extrinsic factors, may, however, be due in part to the guidelines of the ICH E5 itself, particularly Section 3. Section 3 describes when bridging and additional studies may be called for and focuses primarily on describing the types of ethno-bridging or clinical trials that may be necessary, depending on how "sensitive" to ethnic differences a new drug is thought to be. It focuses primarily on intrinsic factors, and all but ignores any extrinsic factors (ICH 1998: 3-6). In fact, outside of their inclusion in Table 1 and definitions in the glossary, extrinsic factors are all but ignored and seem to be accorded very little importance in ethno-bridging studies in the ICH E5. One result of this is that opportunities to examine and explore the complex feedback loops between intrinsic and extrinsic factors that are undoubtedly occurring during drug trials have not been exploited. Instead, the potential data and insights that a more nuanced exploration of these trials could yield are being lost due to this static view of "ethnic bodies".

This is particularly interesting in the case of those ethno-bridging studies conducted for drugs that aim to be marketed in Japan. The Japanese have long had their own ideas concerning "local biology", which are linked to how they think about not just individual bodies and health, but also their national identity. In her work on illness and culture in Japan, Ohnuki-Tierney (1984) describes the idea of "*taishitstu",* which can be loosely translated as "one's inborn constitution" or "one's inherent nature" (Ohnuki-Tierney, 1984). It corresponds closely to the use of blood type in both Japanese biomedicine and popular culture to describe a person's personality, behavioral characteristics, and propensity toward certain types of illnesses (Ohnuki-Tierney 1984:77). It is thought that *taishitsu* has a profound effect on how well a person reacts to external factors, such as drugs, herbs, the weather, seasonal fluctuations, diet, exercise, alcohol, tobacco use, and even everyday or major life events. *Taishitsu* is a central concept in Japanese culture, and as Ohnuki-Tierney points out, "the Japanese must understand their *taishitsu* because health is a somewhat ephemeral condition that represents a delicate balance between the *taishitsu* and external stimuli" (Ohnuki-Tierney 1984:56). Any weaknesses in a person's *taishitsu* must be carefully considered and protected against in terms of diet, behavior, and external stressors that he/she might encounter. The idea that health is a balance, that there is no single "perfect" state of health and that health is in constant flux, depending on factors in the environment as well as within one's own body, embraces the notion of a feedback loop between biology and culture, diet and the environment, and so on. Relevant to our consideration of ethno-bridging studies, *taishitsu* is used, both at the level of the individual and at the level of the collective Japanese body. Japanese doctors often use the argument that *"Nihonjin no*

taishitsu ga chigau" or "Japanese bodies are different" to support their dismissal of clinical study data generated in the US or their own non-use or altered use of Western drugs (Lock and Nguyen 2010: 88).

Whether or not "*taishitsu ga chigau"*is biologically based or a form of cultural essentialism on the part of Japanese doctors and others is a contested issue in fields ranging from Japanese studies, anthropology, medicine, to international politics, transnational trade and economics, to name just a few. In his analysis of a Japanese doctor's explanation for why there has been slow uptake of SSRIs in Japan, Kirmayer, for example, notes that the doctor:

> "Slides easily between notions of a distinctive Japanese biology or physical constitution and of a unique culture or value system….However, the confident assumption that Japanese are fundamentally different from non-Japanese is not based on research studies but reflects a form of cultural essentialism that became common in Japan during the Meiji era in a genre of literature termed *Nihonjinron* that celebrated the uniqueness of the Japanese people. Many Japanese are comfortable with the notion that they are somehow distinct from other peoples, not only because of their culture but in the very substance of their brains and bodies. Although there may well be local biologies, this popular literature on the distinctiveness of the Japanese is ideologically driven" (Kirmayer 2002:301).

Kirmayer notes that "local biologies" might exist in Japan, but states that while there may be important differences in drug metabolism and effects "due to genetic polymorphisms and diet or other environmental factors," he goes on to say that "in most cases these remain to be established" (2002: 301). Thus, he essentially dismisses Japanese ideas of local biology as little more than cultural ideology perpetuated over the last several hundred years, and which have very little scientific basis. It can be tempting to dismiss Japanese assertions about the distinctiveness of their physical and genetic characteristics as purely ideologically driven and little more than attempts to reify notions of Japanese uniqueness. However, a plethora of scientific, medical, and pharmaceutical data suggests

that there are very real differences between "racially" defined groups in terms of the biological trajectories of some diseases as well the effects of some drugs (Gravlee 2009). Variations in the way some classes of drugs affect different groups of people are due primarily to genetic polymorphisms, and these have become the primary focus of pharmacogenomic research (Meyer 2002). There is also a significant body of work that points to differences in how Japanese, other non-Japanese Asians, and Westerners are affected by some drugs, which provides additional support for ideas of distinct differences in Japanese bodies (see Jhee et al. 2006 for an overview of this literature).

It is beyond the scope of this paper to fully review the medical and pharmaceutical literature to date that details the many ways in which pharmacokinetics can be altered in response to ethnic factors (for a review of this literature see Jhee et. al. 2006; and Ruckle 2009). However, a brief discussion of one of the key genetic differences around which much of the data on this topic has centered will help us to understand how inter-ethnic group differences at the genetic level can greatly influence the pharmacokinetics of drugs. Currently, the majority of genetic differences (polymorphisms) that have been studied in the context of medical and pharmaceutical research center around degradative enzymes such as cytochrome P450 monooxygenases which are responsible for the body's metabolism of drugs (Jhee et al. 2006:29). This system, which is composed of 74 separate P450 gene families, is what determines how the liver will conduct its metabolic functions (Van de Weide and Steijns 1999; Jhee et al. 2006: 65). Cytochrome P450 enzymes conduct several oxidative biotransformations, such as dealkylation, hydroxylation, oxidation, and deamination. Biotransformations by CYP1, CYP2, and CYP3 account for the majority of exogenous compounds while the other enzymes largely metabolize the

endogenous ones (Jhee et al. 2006: 65). CYP3A enzymes are the most important in this function. In fact, CYP3A4 is involved in the metabolism of nearly half of all drugs and its presence in the gastrointestinal tract is suspected to be one of the primary reasons for the poor bioavailability of many drugs. CYP2D6, on the other hand, is implicated in the metabolism of about one-quarter of all drugs (Benet et. al. 1996; Jhee et. al. 2006). Given the role of these enzymes in the metabolism of drugs, an increase or decrease in their functional capacity could greatly impact the body's ability to metabolize drugs and significantly alter the pharmacokinetics associated with a specific drug or class of drugs (Jhee et. al. 2006).

Allelic variations are common in cytochrome P450 enzymes, especially across racial and ethnic boundaries (Jhee et al. 2006:65). Polymorphisms, commonly referred to as SNPs (single nucleotide polymorphisms), have been identified in several CYP enzymes, including those for the CYP2D6 and CYP2C19 genes. As noted above, genes in the cytochrome P450 monooxygenase system, such as CYP2D6 and CYP2C19, are closely related to the liver's metabolic functions. This is why, with allelic variations most common in this system, we see the greatest difference across population groups, which correspond in some cases to racial groups, in the hepatic metabolism of drugs (Jhee et al. 2006: 66). These SNPs are extremely important in terms of enzyme activity, because they can either cause an enzyme to no longer be produced (deletion) or can heighten the level of enzyme production (gene duplication) (Jhee et al. 2006). These SNPs help to determine whether or not someone will be a poor, intermediate, extensive, or ultra-rapid metabolizer. While there are several distinct metabolic phenotypes that can occur, the frequency of these phenotypes differs greatly between some populations. Table 3 shows

four of these metabolic phenotypes according to frequency in Asians, Caucasians, and Blacks. This can affect how individuals metabolize drugs and can have a profound effect on clinical applications (Jhee et al. 2006:67). CYP2A6, a principle hepatic enzyme that converts nicotine into cotinine, helps us to see how there are genetic differences that are distinct to the Japanese, and these can have an impact on the ways that drugs affect Japanese individuals. As Table 4 shows, there is a substantial difference in enzyme activity across ethnicities, and Asians, particularly Japanese, have a strikingly high CYP2A6*4 allele. This means that they are homozygotes for this allele and have a diminished ability to convert nicotine into cotinine, making them poor metabolizers of nicotine (Jhee et al. 2006). Further, this enzyme is also important in the metabolism of other drugs such as halothane (general anesthetic), valproic acid (treatment of certain types of seizures), tamoxifen (treatment of breast cancer), and ritonavir (for treatment of HIV/AIDS) (Jhee et al. 2006). Thus, this genetic polymorphism may have other important clinical implications that should be carefully considered in drug development, particularly for those drugs targeted for Asian populations.

Table 3. Relative Frequency of Slow/Poor Metabolizing Phenotypes
(Jhee, Rosenthal, Moran, & Ereshefsky, 2006; Wood & Zhou, 1991)

Metabolic Phenotype	Asians	Caucasians	Blacks
Slow isoniazid acetylator phenotype	7-34%	52-62%	40-65%
Slow debrisoquine	0.5%-1%	5-10%	1-8%
Poor S-Mephenytoin phenotype	17-22%	3-5%	-
Atypical alcohol dehydrogenase phenotype	85-90%	<5%	-

Table 4. Frequency of CYP2A6 Alleles
(Jhee, Rosenthal, Moran, & Ereshefsky, 2006; Nakajima, 2001; Oscarson, 1999a; 1999b)

Allele	Spaniards	Japanese	Chinese
CYP2A6*1A	66.5	42.4	43.2
CYP2A6*1B	30.0	37.5	40.6
CYP2A6*2	3.0	0	0
CYP2A6*3	0	0	0.7
CYP2A6*4	0.5	20.1	15.1
CYP2A6*5	0	0	1.0

Local Biology as a Technique of Governmentality and Bionationalism

Given the scientific data on this topic, which we have only just skimmed, it is justifiable for the Japanese government to require ethno-bridging studies prior to a drug's introduction to Japan or in order to inform the conduct of larger Phase 2 and 3 trials within Japan. What we wish to call attention to in this paper is that calls for ethno-bridging studies also serve a biopolitical agenda within Japan. By presenting scientific data that highlights the distinctiveness and difference of the Japanese population and portraying this difference as a static rather than a dynamic form of local biology, the Japanese government is engaging in a process of governmentality which promotes a nationalist agenda. As noted earlier, the MHLW almost invariably requires additional testing for drugs developed outside Japan. Justifications for needing to do so are supported by data on ethnic difference, which are presented as social facts and which situate the government in an apparently ethically defendable position from which they can limit foreign access to Japanese pharmaceutical markets in the name of protecting Japanese citizens. In this way, access to the Japanese Pharma market is controlled by the government, which has established a separate clinical trial pathway for foreign pharmaceutical companies. Essentially, local biology becomes a technique of governance through which the Japanese state is able to "conduct the conduct" of foreign pharmaceutical firms and the Japanese people (Dean, 1999).

Despite having signed the ICH E5, Japan thus continues to exercise biopower over its citizens, through the production of knowledge about Japanese bodies enabled by a discourse on drug compatibility (and incompatibility) articulated by policy makers and doctors alike. The state exercises governmentality at the site of the body by restricting

the Japanese public's access to Western drugs, drugs that Western manufacturers intended for allegedly universally exchangeable bodies. Doctors and policy makers in Japan justify such restriction by using rhetoric that emphasizes risk. Additional tests are deemed necessary in order to protect the Japanese people from harm and to reduce the potential risk that being exposed (contaminated) to drugs perceived to be designed for "other" (i.e. western) bodies poses. Seen in this way, state regulation and surveillance of the global pharmaceutical market is part of a larger medical citizenship project that is hegemonic and reproduced through the apparent common sense and everyday practice of choosing the right medicines for the right bodies. Further, these regulation activities, whereby drugs become authorized by the state, are an example of pharmaceuticals as "biopolitical artifacts" (Lakoff 2008). Lakoff (2008) has used this term to describe how pharmaceuticals are "technical innovations that pose problems around how life should be understood and managed, and thus provoke novel ethical and political quandries" (Lakoff 2008: 742).

Clinical trials are biopolitical in yet another way as well. Japanese ethno-bridging studies have strict inclusion and exclusion criteria that are tightly controlled by the MHLW. Not only do genetic polymorphisms need to be controlled for, but also those factors related to local biology such as environment, diet, and culture. Japanese participants in ethno-bridging studies who live in the US must provide documentation of Japanese birth and citizenship via passport or visa, and "fill out a three-generation genealogy tree documenting that both parents and all four grandparents are Japanese and

were born in Japan" (Ruckle 2009: 756). This means that only *issei*[10] Japanese are eligible, whereas *nissei* are *sansei* are not. Those with mixed Japanese/non-Japanese heritage are also ineligible (Jhee et al. 2006: 6). There are also stringent guidelines regarding the amount of time an individual can have spent outside Japan, generally no more than 5 years. Of utmost importance is that the individuals who participate in these bridging studies look as much like those Japanese residing inside Japan as possible, with no significant differences in lifestyles. As a result, these studies must be conducted in cities like San Francisco, Los Angeles, and Honolulu, where they can take advantage of large populations of overseas Japanese who have easy access to Japanese supermarkets and restaurants as well as large populations of Japanese individuals (Anonymous expert #1, personal communication 10/8/10; Anonymous expert #2, personal communication 10/11/10). Through designating who is eligible for these bridging studies, which are used to extrapolate data out to the general Japanese public, the Japanese government articulates and defines the boundaries of what it is to be "Japanese" in terms of a national (bio)identity and also is able to show that to be " truly Japanese", has "biovalue".

Biovalue is the "vitality and profitability produced by the reformulation of living processes" (Waldby and Mitchell 2010: 336). The data that is generated by Japanese subjects in EB studies has different biovalue for the different parties (trial subjects, pharma companies, and the state) involved. Trial subjects may gain material, symbolic, and cultural capital through their participation. Overseas Japanese are recruited to EB studies via promotional materials of all kinds. For example, the website of a clinical

[10] Issei is first generation Japanese; Nissei is second generation Japanese, which means the individual was born outside of Japan but his/her parents were born in Japan; Sansei is third generation Japanese, which means the individual was born else where and one or both parents were born outside of Japan but the grandparents were born in Japan.

research organization (CRO) that specializes in EB studies in southern California says, on the first page of their recruitment section for Japanese study participants (which is written in Japanese but translated here) "there is something you can do for Japan from America" (West Coast Clinical Trials Website 2011). By virtue of having the correct (bio)identity, overseas Japanese can participate in the (bio)nationalist efforts of the government by "giving something back" to Japan, showing nationalistic sentiment and loyalty. Their voluntary participation gives them a sense of moral identity and symbolic capital because they have helped their homeland.

For Japanese pharmaceutical companies and clinical trial recruiters, the bodies of "authentic" Japanese have biovalue as data that can be exchanged for money and access to markets. For the Japanese government, the biovalue of subjects is realized in their participation in trials that identify appropriate medicines for Japanese bodies, an act which reproduces the representation of Japan's uniqueness. Determining the (bio)identity of the Japanese people through pharmaceuticalization is an example of pharmaceuticals as biopolitical artifacts (Lakoff 2008) and governance that links state politics to individual practices and biosocial realignment in the name of health.

Ethno-bridging studies that demand proof of efficacy at the site of Japanese bodies contribute to Japanese bionationalism. Bionationalism, according to Wahlberg, "relates to different forms of practice which aim at strengthening the collective vitality of a nation state –as regards its population, culture, economy and ecology - *as a matter of competition*" (Wahlberg 2009: 243 emphasis in original). By engaging with the competition that is inherent in the market of transnational clinical trials and actively creating (bio)identities and then exploiting their (bio)value, the government of Japan

achieves its protectionist goals while simultaneously reproducing a sense of bionationalism. This sense of bionationalism gives the Japanese government the moral high ground to defend its position by citing scientific data on biological differences and by supporting long held Japanese perceptions of local biology re-articulated through claims that EB studies must be validated in Japanese bodies. A strong sense of bionationalism enables the Japanese government to regulate foreign pharmaceutical company penetration into Japanese markets, and yet be seen as a global citizen who adheres to free trade policies. Pharmaceuticals thus become the exception that reminds the Japanese of their uniqueness.

Conclusion

This case study provides insights into a post-modern Japan striving to keep up with the pace of a globalizing world, yet at the same time employing techniques of governmentality and bionationalism based on notions of a uniquely Japanese ethos. A Japanese sense of local biology has long existed in Japan. New perceptions of bioidentity established through discourse on and policy governing pharmaceuticals is more than old wine in new bottles. New representations of bioidentity have emerged to meet new challenges in a high stakes pharma marketplace and a world rapidly becoming interconnected. In such contexts, medical anthropologists have provided compelling case studies that illustrate how local illness categories figure into identity projects (Nichter, 2008). We argue in this paper that pharmaceuticals play a similar role in Japan. Ethno-bridging studies provide a space where identity is negotiated, uniqueness reaffirmed and markets protected. As such, they provide a compelling site from which to base further research on the ways in which local biology is understood at the site of the individual and

collective body and taken up in varying projects in a globalizing Japan.

CHAPTER 2

Flexible (In)Commensurabilities: The Social Process of Constructing Animals as Lab Experiments

> *"I mean, I've seen monkeys in zoos and stuff but the first time I was face to face with a monkey in a lab, to see their facial expressions – to see their eyes and their faces, it was as if I was looking into another person."*
>
> Scientist 04

Introduction

The social process of commensuration enables "the transformation of different qualities into a common metric (Espeland and Stevens 1998:314). Commensurability is a useful lens through which to understand how seemingly very different objects can be collapsed down to a few, often very basic, common characteristics, and thus transformed into objects which can be compared. In the biomedical sciences, commensurability is a key component of the randomized controlled clinical trial, the gold standard of modern biomedical research. Historically, human clinical research has focused on white men as the "average person," excluding women, diseased individuals, and minorities.[11] Scientists have focused on these populations in an effort to eliminate potential confounding factors that come from individuals with dissimilar bodies and produce studies that are as generalizable as possible to the general public. Prior to studies in humans, preclinical studies using animal bodies must be performed. As in human clinical trials where study subjects' defining characteristics must be "flattened" in order to allow comparisons within and across groups, the construction of animals as "suitable" proxies for human bodies in biomedical research similarly requires that animals be made to be

[11] Although in recent years various groups have successfully lobbied for greater inclusion of diversity in clinical trials (Epstein 2007), the objective of clinical research studies remains to be able to compare results among and between participants and ensure data that are generalizable to the greatest number of people.

commensurate for humans. Despite the focus on the need for a standardized human subject, much less attention has been paid to these issues in preclinical research.[12] The study of clinical research in the social sciences has followed this focus as well. The majority of social science scholarship on clinical trials that considers commensurability typically focuses on human bodies as they pertain to Phase 1-4 human clinical trials (Sunder Rajan 2007; Epstein 2007; Petryna 2009; Kelly and Nichter 2012, Lock and Nguyen 2010). Very little consideration has been given to how *pre*-clinical studies using animal bodies as proxies for human ones are framed and positioned. And yet the concern around human differences in clinical research, both in biomedicine and the social sciences, would seem to suggest that using non-human animals would warrant concern as well. These spaces provide a unique opportunity from which to explore the role of multi-species interactions and flexible ways in which bodies are constructed in biomedical research. Thus, this paper aims to contribute to this literature by exploring the flexible ways in which scientists assign value and meaning to different animals, in particular nonhuman primates (NHPs), and how they construct them as objects of scientific and biomedical inquiry, data generation, and knowledge production.

Lock and Nguyen describe commensurability in human clinical trials, as that which

> "allows people to be sorted into standardized groups and populations because their biology is assumed to be the same. This provides the grounds for meaningful

[12] The NIH recently announced new guidance and policies that will increase the use of female sex cells and animals in preclinical research (Clayton and Collins 2014). These policies are in response to data showing that women and men are affected by drugs differently and that women experience higher rates of adverse effects from drugs compared to men (Franconi et.al. 2007). It has also been suggested that the inadequacy of preclinical researchers' analysis of study data by sex could be contributing to the rise in the irreproducibility of animal study results. And reproducibility of science is one of the hallmarks of science's claims to objectivity and truth (Collins and Tabak 2014; Landis 2012).

> comparisons to be made among them. Comparing apples from different orchards generates a more precise form of knowledge – about orchards, soils, farmers, or varieties – than say, comparing apples and oranges. Such comparisons are the basis of modern, scientific biomedicine" (2010: 176).

Importantly, this is more than just a scientific endeavor. Commensuration is a complicated, sometimes contradictory, and almost always emotionally-charged set of social processes (Espeland and Stevens 1998). Two key components of commensuration, especially in relation to bodies in scientific studies, are flexibility and valuation. The multi-dimensional and flexible ways in which animals can occupy and move between multiple categories simultaneously is dependent on humans' perception of animals' connections to human social worlds, and has been the focus of much inquiry in recent years (Herzog 2010; Joy 2011; Shir-Vertesh 2012[13]). Additionally, much of this is tied to the ontological categories through which humans understand and interpret the natural world (i.e Merleau-Ponty 1995; Valeri 2000; Douglass 1966). Animals then, are flexible in terms of how society thinks about, engages with, and uses them.

In examining flexible bodies, the scientific experiment provides a useful platform. In her work on the topic, Martin notes that the body today is viewed as:

> "a fluid, ever-changing body, a body containing turbulence and instability, in constant motion, a body is the antithesis of a rigid mechanical set of parts…it is in delicate relationship to its environment, a complex system nested in an infinite series of other complex systems" (Martin 2000: 123).

[13] This is by no means an exhaustive list, as research into animal-human relations, animal emotions, cognition, and sentience have exploded in recent years. In fact, Shapiro (2010) notes that in the last decade, hundreds of key texts have been published in the field of human-animal studies.

Flexibility, particularly as it relates to the ability of the body as a complex system to accommodate and adapt to its environment, is critical to understanding how scientists understand, construct, and advocate for or against the use of animals as proxies for human bodies in research. Flexibility proves to be a key tool that both 'produces' animals as *similar enough* to be used as stand-ins for humans while simultaneously undoing this work by creating animals as *different enough* from humans such that animal bodies can be justified as expendable. Only through this simultaneous, antagonistic process can animals be constructed in a way where they are defined as similar enough to humans to yield important data to make comparisons and predictions, yet sufficiently different enough from humans such that their use in risky, painful, and often fatal experiments is warranted.

Another key element in the social process of (in)commensuration of animals for humans in science is valuation. Espeland and Stevens note that the making of incommensurables happens when "we deny that the value of two things is comparable" (1998:326). However in order to justify the use of animals in the scientific apparatus, they must be assigned a value lower than that of humans. Their bodies are useful because of their similarities to humans, but they can also be used in experimentation because of their very differences, which do not warrant the same ethical consideration as humans. Thus, these differences imbue them with a biovalue that is not equivalent to that of humans.

Biovalue is the "vitality and profitability produced by the biotechnical reformulation of living processes" (Mitchell and Waldby 2010: 336). In the case of animals in science, their bodies are used in various ways to generate data, knowledge,

and profits for those engaged in the scientific economy of biomedical research. Animals for experiments must be purchased, cared for during their life in the lab, and either retired or euthanized at the end of a study – all at a cost to research labs. In this way, their bodies have been made into commodities and assigned a biovalue. However, not all animal bodies are assigned the same biovalue. Some, such as the great apes, have biovalues that render them so similar to humans that their use in scientific experiments in the United States has been made nearly impossible (Reardon 2015; Fleur 2015)[14]. Others, such as mice, are on the other end of the value continuum. This is despite the fact that we share 99% of our DNA with mice (Sanger Institute 2002). Thus, this dichotomous assignment of value to animal bodies and the way they are able to move flexibly into and out of categories, provides a rich opportunity to explore the ways in which animal bodies are constructed for use in biomedical research.

Background

Context for Research

Data reported here are part of a larger, ongoing research project exploring the body in science from a multi-species perspective – human, animal, and microbial. As a part of this larger project, I conducted research on the use of nonhuman primates (NHPs)

[14] In late 2011, the National Institutes of Health (NIH) made the decision to suspend all grants for biomedical and behavioral research using chimpanzees based on a report by the Institutes of Medicine. This report, which had been commissioned by the NIH, noted that "while the chimpanzee has been a valuable animal model in past research, most current use of chimpanzees for biomedical research is unnecessary" (NIH 2011). Eventually, the NIH decided to retire all but fifty of its chimpanzees from research. Fifty chimpanzees were kept for "emergency" research on an epidemic such as Ebola. However, in late 2015, the NIH announced that it would retire the remaining fifty chimpanzees and end all funding to research programs using chimpanzees. Importantly, however, this did not mean that all chimpanzee research in the US was ended, as several hundred chimpanzees are held by private biomedical research corporations around the country. However, in June 2015, the US Fish and Wildlife Service gave research chimpanzees endangered-species protection, a designation only provided to wild chimpanzees prior to this. This new protection prevents scientists from engaging or stressing chimpanzees for research unless they can show that it will have benefit for wild chimpanzees. It should be noted that some behavioral research has been allowed to continue.

in biomedical research in order to explore the ways in which animal bodies used in biomedical research are constructed, understood, and negotiated by scientists, lay persons, and activists (both pro- and anti-animal research). This field has become so fraught with contention, animosity, and mistrust among all groups that there is little room for any dialogue. Unfortunately, this lack of dialogue is harmful to everyone involved, including the laboratory animals, the general public who will use drugs and devices being developed, and scientists engaging in these experiments. As such, I conducted this research in order to explore the views of various stakeholders and understand the ways in which they negotiate this contentious terrain in an effort to illuminate areas that might serve as potential places from which to open dialogue and communication. Therefore, this work is grounded in phenomenological approaches to understanding the social construction of the body in science and the role that it plays in, and impact it has on, scientific knowledge production.

NHPs are the focus of this research given that "animals in research" is too broad. Additionally, this study focuses on NHPs because of the genetic similarities between NHPs and humans.[15] Given this genetic closeness, and their longstanding use as stand-ins for humans in preclinical studies, NHPs offer a fertile ground from which to understand the ways in which animals are constructed, or not, as proxies, for humans in biomedical research.

At the time this research was conducted in 2012, the National Institutes of Health (NIH) was in the process of retiring its chimpanzee population from research and had suspended all grants for biomedical and behavioral research with chimpanzees due to an

[15] Chimpanzees, bonobos, macaques, and humans share 93% of their DNA (Gibbs et. al. 2007), with chimpanzees and bonobos being the closest to humans, sharing about 99.6% (Prufer et. al. 2012).

Institutes of Medicine (IOM) report (see footnote #4). In making the announcement in late 2011, the head of the NIH stated that chimpanzees, as humans' closest relatives, deserve "special consideration and respect" (NIH 2011). Given the considerable attention this issue received at the time from media, scientists, academics, and the lay public, focusing on the perceptions, understandings, negotiations, and contestations around NHPs in biomedicine provided a unique opportunity to tap into much of this discussion and interest around this issue at the time. Further, it should be noted that there has been an ongoing public debate about the use of animals in biomedical research testing for many decades. Discussions around the IOM report, NIH decisions, and subsequent work by other government agencies related to the use of NHPs in biomedical research (see footnote #4) reignited these debates for scientists, the public, and activists on both sides of the issue. As such, these events and the debates around them provided an important contextual element for the conduct of this research.

There is a long history in Western social sciences of taking up the issue of animals and human interactions with them, dating back to ancient Greece. While Pythagoras argued for respect of animals based on his idea that reincarnation was cyclical between animals and humans (Steiner 2005), Aristotle disagreed with this saying that animals lacked the ability to reason (Sorabji 1993). Aristotle also put forth the first taxonomy of animals that placed humans at the top and plants, lacking consciousness, all together separate (Sorabji 1993). Later, other theorists such as Aquinas, Descarte, Locke, and Kant focused on the ethics of humans' use of animals. Their arguments focused on animal autonomy, consciousness, will, and morality in order to justify humans' use of animals (Harrison 1992; Nash 1989; Kant 1956; Kant 1993; Regan and Singer 1989).

Aquinas, Locke, and Kant also felt that humans had an obligation to rebuke the cruel treatment of nonhuman animals, not because it was wrong *per se* but because it could negatively impact the human who was inflicting the cruelty (Kant 1956; Kant 1993; Regan and Singer 1989). Given its long history of using animals to understand human culture and distinguishing the "other" and its usefulness and necessity in constructing the "self," anthropology is uniquely positioned to offer important perspectives on this topic (Lacan 1968; Low 1996; Fabian 1990). Theoretical examinations of the self and other have naturally extended anthropological inquiry into animals and animal-human relationships. Historically this has focused on the materiality and functionality of these relationships and the boundaries created by humans in order to categorize animals into various domains (Harris 1966; Rapaport 1967; Durkheim and Mauss 1963; Evans-Pritchard 1940; Geertz 1972; Leach 1964; Levi-Strauss 1963; 1969; Sahlins 1976; Valeri 2000). In trying to understand the binaries and categorization various societies place animals into, anthropologists have long cast their gaze upon those animals marked as edible or inedible and the rituals and taboos around the preparation of certain animals as food (Douglas 1966; Valeri 2000). More recently, anthropologists have begun to explore the role of animals in modern society (Shir-Vertesh 2012) and the ways in which we understand and incorporate them into our lives as pets, cherished companions, and family members (Shir-Vertesh 2012).

However, while animals as food and pets have been critically examined in the social sciences and popular literature and media (Herzog 2010; Joy 2010; Shir-Virtesh 2012), the use of animals as laboratory experiments for cosmetic and biomedical research testing has garnered considerably less attention, especially in anthropology. These

relationships are arguably one of the most intimate of all animal-human relationships, in which animals act as proxies for the human body in order to determine whether drugs and cosmetics are safe to be tested on and/or used by humans. There are likely many reasons that this aspect of the human-animal relationship has gone under examined in anthropology. This includes biologicaland evolutionary anthropology's own history of using animals, especially our closest genetic relatives the great apes and other non-human primates, in pursuit of scientific knowledge. That this topic has been left largely unexplored speaks to our difficulty in acknowledging our often deeply conflicted, nuanced and complicated understandings and negotiations around animal-human relationships.

The Clinical Trial Apparatus

While this paper focuses on preclinical research studies, understanding the drug development process and the importance of commensuration as a component of study design along all stages is useful. Prior to preclinical research studies in animals, in vitro studies are conducted to identify, formulate, and test compounds to be used in animals where the goal is to determine safety, toxicity, efficacy, and dosage for first-in-human studies. Importantly, these studies also assess carcinogenicity, mutagenicity, teratogenicity, and how the drug is excreted and absorbed. The FDA requires that drugs be tested in at least two animal models prior to testing in humans to account for differences between the physiology of the animals and humans (CDER 1998). However, this does not mean that only two studies are done in animal models prior to the drug moving into human studies. On the contrary, dozens of pre-clinical studies will be done in animals in an effort to collect enough data to justify first-in-human clinical trials.

However, because of cost, feasibility, fast life course, and political/social climate regarding the use of animals in research, mice and rats are most often used to develop a dossier of data that can then justify studying the drug in another animal model. NHPs are generally the least used in research studies because of cost, time, slow life histories which can result in long periods of time to see results in these animals, and the contentious political/social climate around their use.

Following studies in mice or rats, scientists are specifically looking for an animal model that will generate the best and most translatable data that can be used to support further study of the drug in humans. Therefore, animal models at this point are chosen based on how similar they are to humans in terms of the specific organs or body systems that the study drug's mechanism of action is targeting. For example, if the drug being tested is to treat cardiac issues, a canine may be used given the similarity of human and canine hearts. For respiratory illnesses, ferrets are often used, and for neurological diseases, primates. Testing in the preclinical phase can be either short (two to three weeks) or long (ranging from a few weeks to several years). Generally speaking, the preclinical phase of testing can take between ten and fifty studies and last up to several years. Once enough information has been collected, the FDA reviews and determines whether tests in humans can proceed (See Figure 1).

Figure 1. Clinical Trial Pipeline

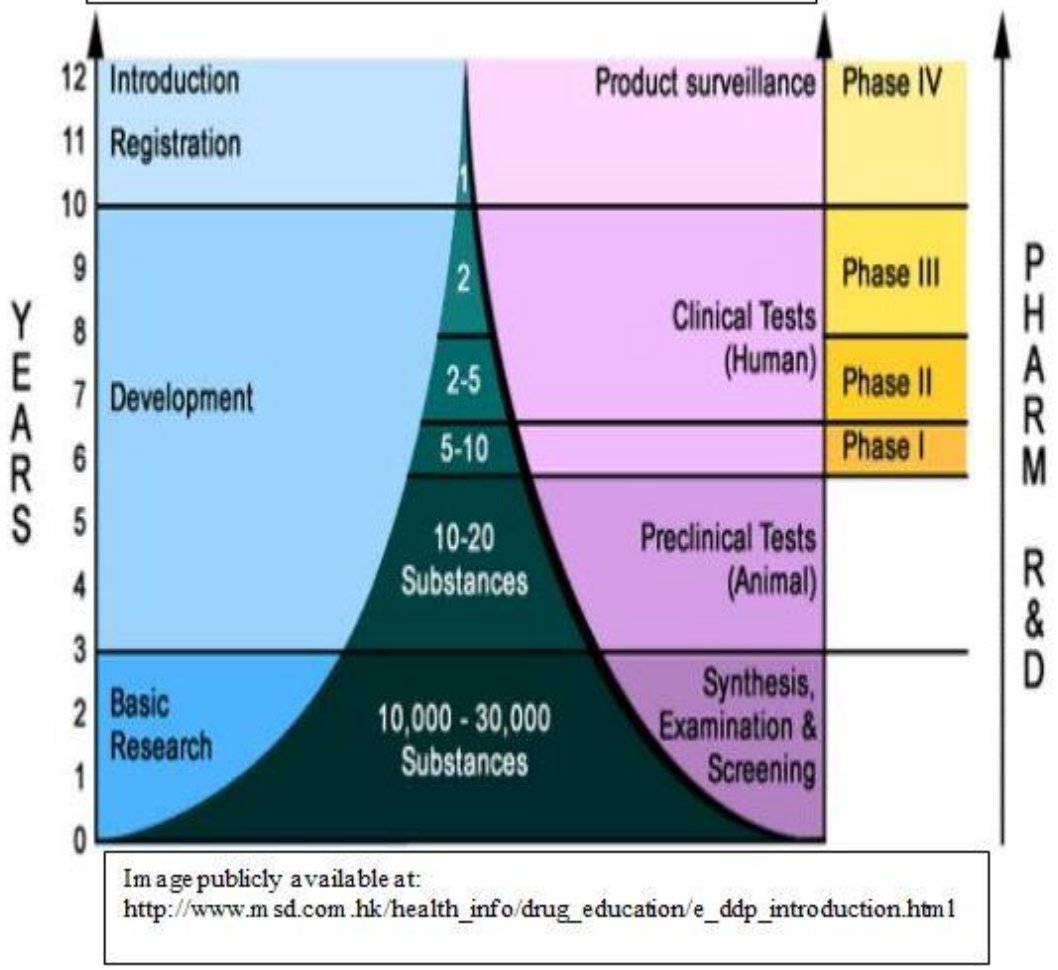


Image publicly available at:
http://www.msd.com.hk/health_info/drug_education/e_ddp_introduction.html

If tests in humans are allowed to proceed, a first-in-human Phase 1 clinical trial will occur. Phase 1 studies are conducted using healthy volunteers except in the cases where the drug is known to be toxic such as in cancer studies. Done primarily to assess the safety of a drug, particularly how it is absorbed, metabolized, and excreted in healthy humans, they are generally very small, enrolling between 20-80 healthy individuals. Phase 2 clinical trials are often randomized studies of several hundred people who are sick with the targeted disease. These studies asses a drug's safety profile, including side effects and tolerability and can provide preliminary data on a drug's efficacy. Phase 3

clinical trials are conducted to determine a drug's efficacy compared to a placebo or a comparator, which is the accepted as standard medical treatment at the time. They also serve to generate information about contraindications and other potential benefits and/or harms such as adverse reactions. Phase 3 clinical trials enroll several thousands of participants who are ill with the disease a drug is designed to treat (See Figure 1). Following successful Phase 3 studies and subsequent approval by the FDA, a drug can be marketed to the general population.[16]

At all points along the preclinical and clinical trial process, commensuration of bodies is a crucial component of study design. Standardizing human bodies across these categories is important for clinical trials as they are seeking to develop evidence on the ability of a drug to treat the "average" person in a population and make claims about its ability to treat those in the general public as opposed to a subset of the population. Given the importance of this issue to human-human studies, the process of commensuration in animal-human studies, which are the building blocks of clinical research, should be further investigated to understand the social processes through which it occurs.

Methods

Scientists were identified using purposive sampling at the suggestion of two primatologists serving on my dissertation committee, and web and literature reviews. Additionally, four scientists were suggested by interviewees. Purposive sampling was

[16] At this point drugs enter the final stage of drug testing, Phase 4 clinical trials. This phase is more generally known as "post-marketing surveillance studies" and are conducted post-regulatory approval on marketed drugs. This is not an active testing phase of drugs, but requires the active participation of the doctors who prescribe the drugs and their patients who are taking them to report any effects they are experiencing as a result of taking the drug. The goals of this phase of testing are to compare a drug with other currently marketed drugs, to monitor long-term safety and effectiveness, including patient acceptability, and to understand the costs vs. benefits of the drug compared to other marketed therapies for the same indication. These trials take anywhere from two to ten years to conduct and involve thousands of diseased subjects.

used in order to identify individuals that conduct research, both invasive and noninvasive,[17] as well as both in lab and field settings, with a variety of NHPs. The type of NHPs studied by scientists in this sample include marmosets, titi monkeys, rhesus macaques, Japanese macaques, bonnet macaques, vervets, chimpanzees, bonobos, and orangutans.

Thirty scientists were contacted, and of those, twenty-two participated in an interview. In-depth semi-structured interviews were conducted with twenty-two scientists, those who support and/or conduct invasive biomedical research with NHPs (N=15) and those research scientists who do not (N=7).[18] Interviews were conducted in-person when possible, otherwise by phone and generally last an hour in length, although several were two or more hours long. Interviews were transcribed and analyzed using a phenomenological approach attentive to the interviewee's background, current work, specific NHP model used, invasive or noninvasive research, lab vs. field setting, and interview context. Themes emerged from the data de novo, using a grounded theory-like approach to coding, and were not imposed using pre-determined themes or codes. In this way, salient ideas and themes from across the interviews were able to come into relief and "speak" to one another. At the beginning of each interview, scientists were asked

[17] The term "invasive" research here is defined as research that manipulates an animal in a research setting through means of injecting substances into its body, conducting surgical procedures on the animal to understand a drug's effects, and/or attachment or insertion of devices into the animals' bodies. In this sample, captivity is treated as an "invasive" procedure and therefore observational studies of captive primates is included in the "invasive" category. "Noninvasive" research is defined as research conducted without manipulation of the animal through observations in the wild (non-captive research). Some of the scientists in the noninvasive sample at one point in time conducted invasive studies with animal species, but no longer do. It is also important to point out that these definitions are not universally understood or used in the scientific literature this way, and some scientists in this sample would not categorize themselves as "invasive" researchers. Nevertheless, for the purposes of this research, this is the way in which scientists were categorized at the beginning of the sampling process and thus how the results are reported here.

[18] Guest et. al. (2006) have shown that in purposive sampling of specifically targeted populations or experts, data saturation generally occurs within 12 interviews and can occur, in very specific or narrowly defined groups of people, in as few as six interviews.

about their personal history working with animals, how they became involved in their current work, their training, and any formative experiences in the lab or field that might have impacted their views on the interview topics. Several scientists elected to go back all the way to childhood to describe their connections to their work while others started their stories in college, with their formal training.

Key to my analysis of the ways in which scientists understand, negotiate, and describe their work with NHPs in science is the use of multipositionality and multivocality as a lens to understand the dichotomous and sometimes conflicting views that individuals simultaneously hold on these topics. Multivocality (Bakhtin 1981) is useful tool in understanding scientists' viewpoints on these topics because it suggests that our utterances are best understood in the context of an exchange with other people in our lives (who are both seen and unseen). Our utterances on issues are in response to the imagined positions of others, and therefore are anticipatory in relation to what they might say. Utterances are embedded in an ongoing dialogue with others, and these others can be either people or positions. The dialogical self is conceived of as a dynamic multiplicity of positions in the mind, and these are in constant conversation with the utterances around them. Multivocality as a tool, then, can help resolve situations where there are instances of apparently contradictory "voices" within a single speaker or utterance. [19] It is particularly useful as a lens in this study in order to understand the contradictory statements scientists often made within a given interview. It helps reveal the complex and nuanced work that scientists engage in as they work with these animals, giving credence

[19] The description here of multivocality and Bahktin is taken directly and nearly verbatim from personal communication (email) with Dr. Dana Osborne (4/24/16).

to the ways in which their own backgrounds, histories, and experiences shape their thoughts and feelings on these issues.

is particularly useful in understanding the ways in which people in this study move fluidly between ideas about and their relationships with primates, their views on their similarities and differences in terms of their physiologies and theory of mind, and their engagement in anthropomorphizing animals. The multipositionality that emerges from these conversations must be viewed in relation to the researchers' backgrounds and ultimate motivations for doing this work. In so doing, they add a rich dimension to this data through an analysis of the complex ways in which scientists engage with NHPs in their work.

Many scientists approached for this study did not easily grant interviews, citing the political climate surrounding animal research today. However, those who did grant interviews noted their deep commitment to increasing awareness among the public about their work and their commitment to a "greater good." They were eager to let others know about the importance of their work for both animal and human lives, thoughtfulness with which they engage with their research animals, and the difficulties, both internal and external, they often encounter. As the scientists who conduct this work are a small group of highly specialized individuals, no names or other identifying information about the specifics of their work, workplaces, or backgrounds have been used in order to protect their anonymity and safety. Additionally, as an added protective measure, I have elected to use the neutral pronouns they/them/their in order to further conceal the identities of my informants.

Emergent Themes

This paper focuses on three main themes that emerged from interviews with scientists and details the invisible and yet powerful work they engage in to make animals (in)commensurate for humans. Although other themes did emerge in these interviews, the three reported on here most clearly illuminate the myriad ways in which scientists understand and talk about their work, but also both the internal and external friction and conflict they experience on a daily basis as they engage in this work. These themes include a focus on the physiological and biological similarities and differences between NHPs and humans, theory of mind (ToM), and the anthropomorphizing of animals.

First, in an effort to describe the similarities and why animal bodies are appropriate proxies for human bodies, scientists rely on discussions of the biological and physiological ways in which animals resemble humans. Physiological similarities are used to explain why animal bodies are so important and necessary for science. The focus on the similarities between humans and nonhuman animals is of paramount importance to the conduct of preclinical research with animals. In fact, it is *the* reason that animal research is carried out and serves as the basis for all drug research. This can be seen in the quote below, taken from the facts page of the "Speaking of Research" website, an international advocacy organization focused on providing accurate information "about the importance of animal research in medical and veterinary science" (Speaking of Research 2016).

> "Although humans and animals (technically "non-human animals") may look different, at a physiological and anatomical level they are remarkably similar. Animals, from mice to monkeys, have the same organs (heart, lungs, brain etc.) and organ systems (respiratory, cardiovascular, nervous systems etc.) which perform the same functions in

> pretty much the same way….There are minor differences, but these are far outweighed by the similarities. The differences can give important clues about diseases and how they might be treated – for instance, if we knew why the mouse with muscular dystrophy suffers less muscle wasting than human patients, this might lead to a treatment for this debilitating and fatal disorder."

In this quote, aimed at general public, scientist advocates highlight the "remarkably similar" bodies of animals and humans, which then signal why they are so important, and is justification for their use in science. Scientists and others who support the use of animals in research point to the reality that much of the preclinical research done in animals is unethical to do in humans (Conn and Parker 2008). This is because it often requires vivisection and autopsy work, but also because often there is not enough data to predict how a drug will act in the human system. Thus, because early drug research cannot ethically be conducted on human subjects, and because human and nonhuman animals' bodies are, as noted above, "remarkably similar," animals provide ideal conduits through which to conduct this work. The quote above also importantly points out that difference in bodies and the ways in which they respond to disease can provide useful clues for human health. This use of difference was also reflected in interviews with scientists in this sample. They also reveal that while similarity is used to make animals commensurate to human bodies, differences are used to separate animals and demarcate them as simultaneously incommensurate.

The second theme emerging from this research is theory of mind (ToM). ToM is used to delineate differences and similarities between humans, apes, and lower order primates. ToM suggests that an individual can ascribe a mental state to both him/herself as well as others (Premack and Woodruff 1978) and have "mental state concepts such as

'believe,' 'know,' 'want,' and 'see,' and that individuals with such concepts use them to predict and explain behavior" (Heyes 1998). Since the 1970s ToM has been explored widely in many species, particularly chimpanzees and corvids (Emery and Clayton 2004) and continues to be an extensively studied and debated topic among primatologists, cognitive scientists, biologists, and ethologists (for a review of this literature see van der Vaart 2014; Drayton 2016). ToM is a contentious issue, particularly with regards to nonhuman animals, primarily because without language or the ability to communicate, it is difficult, some would say impossible, to discern whether nonhuman animals are capable of exhibiting it. One of the main reasons that ToM in animals is so difficult to discern is because we have an incomplete understanding of animals' cognition, mental states, and communication. A major difficulty in discerning whether animals exhibit ToM is the fact that many animals in which it has been tested are adept at stimulus-response learning which is often used in laboratory observation studies of ToM. Hare and colleagues (2000) noted that not only are laboratory studies of ToM problematic for these reasons, but they also do not stimulate the same social problems primates experience in nature, and thus may be inadequate in terms of turning on this this ability in captivity. This in turn makes it difficult to know whether primates are simply learning the behaviors researchers are trying to study in them or if they exist naturally as attempts to understand ToM in animals, particularly NHPs' understanding of gaze, accident vs. intention, perspective, and knowledge (see review in Call 2007). Interpretation of results from these studies has been controversial, however (Povinelli and Vonk 2003), and as such, the debate on how to measure and assess animal ToM continues. part of the cognitive abilities of the animal. Increased naturalistic/field observations would help to inform this

field, but they are often very difficult to carry out (Drayton 2016). Ethologists, primatologists and others have, however, applied various techniques with mixed results in their

In this study, ToM emerged as an important aspect of how animals and humans are made commensurate or not given that, generally speaking, scientists widely believe that certain aspects of human cognition are unique. And, as described by several scientists in this study, the types of similarities and/or shared traits between human and animal cognition can profoundly impact the types of studies done and with which animal subjects scientists are willing to conduct them.

Finally, anthropomorphizing of animals emerged as an important theme in how scientists construct animals and humans as commensurate and how much affinity or kinship they feel they share with certain animals. This in turn impacted their views on and willingness to use certain animals in experiments. Anthropomorphism, the attribution of human traits and emotions to animals, is a key way in which humans, for good or bad, make sense of and teach their children about the natural world (Millman 2016). However, anthropomorphism of animals in science is considered to be a taboo, one that can have seriously negative impacts on the careers of those scientists said to engage in it. This is because it is widely believed that anthropomorphism and those who engage in it lack the ability to distance themselves and engage in objectivity. They are accused of endowing animals with characteristics, ideas, emotions, and abilities that they may or may not possess, and importantly, are often thought only to exist in human animals. In order to accurately understand animal behavior, cognition, and emotion, it is thought that nonhuman animals should be understood on their own terms and through their own

experiences of the world, not through that of humans. But the reality is that humans, as animals, can really only experience and understand the world as humans, and as such, may provide a unique aspect of learning and understanding the animal world that would otherwise not be available in the objective view of science. As de Waal (1997) has noted "to endow animals with human emotions has long been a scientific taboo. But if we do not, we risk missing something fundamental, about both animals and us."

Scientists in this sample are critical of the general public and others who anthropomorphize NHPs in an effort to relate to or understand them in the wild and in captivity. Nevertheless, nearly all scientists in this study engage in some sort of anthropomorphizing. They engage in it order to describe these animals, relate to them, or simply to justify the ways in which they engage with these animals in the lab. However, scientists clearly draw boundaries between humans and animals, perhaps as an attempt to self-correct against what one scientist called the "phobia of anthropomorphizing" in the sciences. However, it also serves as a way to distinctly categorize animals as non-humans. In this way anthropomorphism, like ToM, plays an important role in determining scientists' views of the animals with which they work and to a large extent determines the types of research they are willing to conduct and with which animals.

Thus, as will be described here, these complex themes both illuminate the similarities scientists create between humans and animals and the work they do to demarcate them as separate. Additionally, it is in these spaces where the flexible ways in which animals are treated, valued, and given meaning in relation to human society renders the construction of various animals as (in)commensurate for humans visible.

Results

Physiology and Whole Systems Biology: How Similarity and Difference Are Used in Constructing Animals and Humans as (In)Commensurable

Similarity and difference are both used by scientists to describe the reasoning behind why animals are critical as objects of scientific research studies. The focus for scientists is not to find in an animal an exact replica of a human or the progression of disease as it would manifest in a human, but rather to find a model that is "good enough" (Lewis et. al. 2012). In order to determine whether an animal model furnishes enough key features and representations to be used as a proxy for a human in a research study, scientists emphasized the physiological and anatomical similarities between specific animals and humans in relation to the disease and/or research question under investigation. Similarity is the rationale through which scientists invoked the need for animal bodies in scientific research. In fact, Scientist 16 noted that "it's not how different we are, but how similar we are to any of the other organisms (under study)." Scientists use similarity of animal and human systems as a way to necessitate the use of these animals as proxies for humans and select the most appropriate animal model for the research question. For example, Scientist 17 points out the reasons why specific animals are selected for various studies. They note that when a specific animal system shares key similarities with a human system that is being targeted in a research study, that animal can be defined as the most appropriate model in that scenario. In essence, the animal provides the necessary bridge for scientists to gather necessary data prior to advancing to the next stage of research.

> Sheep are used in research on prenatal influences because they have a placenta…they are very similar to humans, they're a good model for pregnancy related outcome

> measures. Pigs are used a lot for skin because their skin is very similar to humans. So each animal model is appropriate for a different thing, often times.

The idea that certain animals serve as a "bridge" for humans and are therefore necessary objects for scientific study is echoed by Scientist 07 who describes a belief that further cognitive and neuroscientific studies should be conducted in the great apes. In pointing out that scientists can only glean so much data from a macaque brain which is similar but not quite as similar to the human brain as an ape brain, Scientist 07 stakes the claim that because of physiological similarities, certain animals make better models than others depending on the research question. Some animal models can provide critical data that will help bridge the knowledge gap between data derived from a lesser or more distantly related animal species such as a mouse. For Scientist 07, the fact that macaques lack that crucial intermediary physiological trait provides rationale for the use of an animal that is more similar to a human in the ways necessary to answer the research question. It is here that similarity becomes so important. No animal model is ever going to be fail safe, but an animal model that has physiological systems that resemble human ones as closely as possible are able to provide the best approximation for what may happen in the human body. In studies of neurologic disorders, the NHP is almost always the best animal model.

> In neurological terms they (apes) are quite different. They have quite a bit more cerebral mass. And they have a lot more convolutions. So in that sense they are intermediate steps in between macaques and humans.

This idea that no animal model is ever perfect, but that it is important to use animals to provide clues as to how a drug may act in the human body, is discussed by

Scientist 14 in describing a failed drug for a devastating neurological disorder, first tested in rats and then given to monkeys. In this discussion, Scientist 14 stresses two important points. First is the need to use an animal model that will provide data that will allow for the best approximation of how the drug might act when given to humans. It is often the case that no problems or red flags arise when a drug is used in more distantly related animals like mice. However, when drugs are introduced into more closely related animals such as monkeys, this is when problems and issues are often experienced. Animals differ in the ways in which they resemble one another and humans, and these differences can have profound effects on research results. The second is that although cell cultures are an important part of the scientific drug development process, they can only provide a snapshot of the way the drug acts at the cellular level. It can provide basic safety and mechanistic information, but beyond that cell cultures are extremely limited. Using a drug in a living animal model provides researchers an opportunity to see how it will affect the whole animal system, offering pivotal clues as to what might happen if introduced into a living human system.[20]

> "We gave the drug to the monkeys after it had been tested in rats and it had been tested in a cell culture. And everything was wonderful (in the rats). And then we tested it in the monkeys, in the way it was going to be given to patients. And three months after giving it to the monkeys they had developed pancreatic lesions that are similar to pancreatic cancer. And that's the reason that drug was not

[20] The importance of this aspect of pre-clinical studies cannot be stressed enough, for it is in this process that potential side effects, both positive and negative may be seen. Because early detection of side effects will eventually become "expected adverse events" should a human clinical trial ever be undertaken, knowledge gained in these early studies can play a pivotal role in a drug's development and approval. Moreover, if a drug is eventually approved, the entire life of the marketed drug, including prescriptions and recommendations on who should and shouldn't take the drug, what other drugs it might interact with, either positively or negatively, postmarketing studies, side effects reported to doctors by patients, and even law suits may be dependent on this information.

> moved forward. But in a cell culture you're not going to see that."

Thus, scientists' views of an animal model's potential to provide important clues about how a drug might act in a human system play a very important role in how similarities, and ultimately commensurability, between animals and humans are constructed by scientists. Scientist 17 below further supports this idea that living animal bodies provide the best means from which to interpret how a drug may interact in a complex, living system given the lack of basic scientific knowledge available to scientists. They point out that the lack of basic knowledge about the human brain necessitates a way for scientists to generate clues about how a drug might act in the human system. Because so little is known, and cell cultures, computer modeling, and even lower taxa animals such as mice are not good models for the human brain, a bridge is necessary. That bridge is often a NHP such as a macaque. Particularly in neurological research, NHPs serve as this necessary bridge and provide critical data from which scientists can best deduce what the effects might be if used in the human neurological system.

> "I study the brain and the effects of drugs like [ ] on the brain. I can't model that. Why? Because we don't have enough basic knowledge about brain development let alone we don't know the effect of the drug on altering that system. So, we don't have that basic knowledge yet, therefore we can't model appropriately, we need the whole animal."

As such, like Scientists 07 and 14 above, Scientist 17 is making the case that for neurological studies it is most appropriate to use those animals whose neurological systems most resemble humans. To these scientists, the most important consideration is using an animal model whose physiological system(s) most resembles that of the human

system(s) under study. Data from these studies and experiments can be trusted to provide the best possible clues as to whether a drug or device will work in humans. This is especially true for neuroscientists whose work on the brains of NHPs would often not be ethically feasible in human volunteers. Additionally, it should be noted that these nonhuman subjects are not just contributing important safety data, but they are playing a critical role in the process of establishing the ethical feasibility for human trials.

Difference also plays an important role in these discussions and in the construction of animals as simultaneously (in)commensurate for humans. Most notably among scientists in this sample, especially those making the case for use of NHPs in biomedical research, was the idea that animals differ greatly among themselves, even among their own species. As Scientist 17 put it, "animals are different (from one another). So mice are in fact not monkeys. They're differently similar and different to humans." This point was stressed by scientists time and again in their efforts to explain why the choice of animal is so important, and especially by those scientists who use NHPs to describe why their use is so critical. Like Scientist 14 above who describes the failure of the rat model to predict what would happen in a monkey model, Scientist 16 invokes both similarity and difference when describing why NHPs are necessary in their work:

> But testing it (a drug) on a rodent or some non-primate isn't the best solution because, uh, we're dealing with a unique human primate here and some of this work needs to be verified on nonhuman primates. Or a relative if you will.

Scientists repeatedly stressed that not all animal models are created equal, and that in fact, many animal models are not good proxies for the study of drugs depending on the drug's mechanism of action or the physiological system targeted. It is also in these spaces

that differences between animals and humans is used by scientists to reiterate that animals are not, despite their many similarities, humans. Humans and animals may share some important characteristics, but they also differ in important ways. And this point, that animals are different in important ways which can significantly impact scientific data, is critical for drug developers. Scientists repeatedly suggested that these differences are one of the primary reasons why so many drugs never move from preclinical studies to clinical studies in humans (Mak et. al. 2014). In particular, they point to the mouse model, which to many scientists is a very poor model to use. This is particularly true of those researchers conducting neuroscience or cancer research, who suggest that the use of mice may in fact be the reason for falsely negative or positive results in many studies (Mak et al. 2014). Essentially they are pointing out that given the differences in human and mouse physiology, mice are poor stand-ins for humans. As such, other animals should be looked to as a first step in conducting preclinical research. Scientists often point to the differences between animals and humans to stress the ways in which difference matters.

> I think we're relying too much on the mouse model. I think we've already seen decreasing nonhuman primate research and increasing reliance on mice and other models. You'll probably see more failure to translate as a result of that.

Scientist 03, who primarily uses macaques in neurological research, also agrees that using mice in this research is problematic.

> For every neuroscientific question there is the best animal to study it. I think we're way missing the boat by having such an incredible emphasis on rodents. Because they're good for certain things, but not others.

Importantly, these differences and the ways scientists talk about them allow spaces where scientists begin to reduce animals to that which are "similar but just

different enough." It is in these spaces where the justification for the use of animal bodies, because they are not human ones, becomes clear. The differences between humans and NHPs, the fact that humans are doing the research and asking the question, is a clear indicator of humans as the superior species. As Scientist 04 stated:

> "We obviously have higher levels of cognition. Higher intelligence…that's obvious because we're the ones doing the research! Um, we obviously have a higher value, we're going to value the life of a child, an adult more than I value the life of a gorilla or a chimpanzee, forgive me for loving a human more than an animal."

Scientist 05 draws the line even more cleanly when explaining that this value based on a difference of higher intelligence is what justifies animals to be used in research: "Humans are more valuable than animals are. So why not, it makes sense to do research on something that's less valuable than humans." By drawing this distinction, animals are devalued in comparison to humans and rendered unequal, and thus incommensurable with humans. They are simultaneously shown to be useful proxies for humans in science from a physiological standpoint, based on both similarity and difference, but excluded from categorization with humans and thus the rights accorded to our species.

Through this framing, animal bodies are imbued with an important and wide ranging biovalue in the market economy of biomedical research. They have value to the scientists whose work and very livelihoods rely on the use of these docile bodies in knowledge production, to the centers where these animals are bred and sold for research, and to the various academic, corporate, non-profit, and governmental centers where these animals are captively housed for research purposes.

Thus, defining and adjudicating what constitutes both the important and scientifically useful aspects of similarity or difference in comparison of animal and human systems becomes a key component of the work that scientists do in the commensuration process. The focus on animal-human commensurability is on the similarity of characteristics for each individual entity being collapsed into a common metric while incommensurability relies on delineation of differences.

Theory of Mind

When asked to describe what differentiates animals from one another, particularly the great apes from other NHPs, and all NHPs from humans, the most common response among scientists was a "theory of mind" (ToM). ToM differences between animals such as dogs, monkeys, and apes is used to bring some animals closer to humans while simultaneously setting others apart. In fact, it is why some scientists will work with one species of NHP but not others, and at the same time is the logic used by some scientists to claim that some animals are not as "advanced" and therefore should be considered incommensurate to humans. Below, Scientist 08 enumerates gradations in the ways in which NHPs exhibit ToM, with the great apes being at the top of this hierarchy. By noting this variance they describe a hierarchy of NHPs in terms of which are most closely related to humans in this key aspect. Like Scientist 07 above who suggests that apes are neurologically the intermediate step between macaques and humans, Scientist 08 too suggests that apes are an intermediate step between monkeys and humans based on their awareness of their social and physical worlds. This is an important distinction for researchers to be making because, while on the one hand the neurological and other physiological similarities may suggest that they provide the best bridge to extrapolate

what might happen in humans, the acknowledgement that they are so cognitively, socially, and behaviorally like humans raises ethical questions about their captivity and use in research experiments. Importantly, it points out that the same line is being used to rationalize both the use and non-use of these animals in research.

> I've been fortunate to have a lot of field experience, to observe these animals (great ape species) in the wild, and then seeing those animals in captivity, and I really think most animals are sentient. They have an awareness more than themselves of the social, physical environment. There just seems to be a greater, at least in my mind, my impression is that there seems to be a greater, a greater awareness. And even among primates there's a scale of variance, with lemurs on one end of the extreme and great apes on the other, and monkeys in the middle in terms of how one can interact and respond to them.

This use of this dichotomous rationalization is aptly described by Scientist 06, who decided early in their career path to never use any great apes. Today, although retired from research, Scientist 06 still works very closely on a daily basis with NHPs that are used in research facilities. Scientist 06 compares apes, such as chimpanzees, to "primitive aboriginal people" who should not be interfered with by humans in any way.

> I won't participate to anything that contributes to ape research. And I don't hold it against those people that do. Believe me, I think ape research, there is no alternative. That's the only reason that they use apes in research is there is no alternative to some of this stuff. AIDS, and hepatitis and you know, they're curses to humans… and then there is the moral, moral dilemma . . . You know the difference between apes and monkeys is the ability to conceptualize a single point of time in space. So what that gives you is consequence. It gives you a moral identity. It gives you not just a past but a future. You know, its very, very limited in the other apes, other than humans. But it's there.

Further, Scientist 06's description of apes as having a moral identity is what sets them apart from other NHPs, and in their mind, commensurates them, at least to some degree, with humans. This is why Scientist 06 has chosen not to contribute in any way to their captivity, for research, conservation, or in zoos. While they see the necessity, for them it is truly problematic.

The view pervasive in science is that social animals do possess something that resembles a moral structure or system, but due to their less developed cognitive and psychological functioning, their moral systems lack the qualities of those found in human societies (de Waal 1996). While evidence for some of these qualities such as reciprocity, cost-benefit/quantification analysis, punishment of moral code violators, and an ability to remember and/or recall the consequences of bad behavior in the future do exist in several NHP species (Lyon and Santos 2006; Premack 2007; Byrne and Bates 2010; Seed and Tomasello 2010), for many scientists, this evidence is not strong enough to definitively say that a ToM exists in these animals.

For example, Scientist 03 described experiments where monkeys can learn and predict things, but not consider a future point in time. Scientist 03 believes this shows that they are void of the capabilities to generalize and think abstractly, evidence of their inability to consider and / or plan for the future. This ability to understand a past, present, and future was another critical component that scientists pointed to in their descriptions of what sets humans apart from monkeys and apes with respect to ToM. Below we see Scientist 03 actually producing human distinction in terms of how we can conceptualize a future, so much so that it can be an all-consuming thing. Animals, however, live primarily in the now, without concern of a future, making the concept of a future, and

how one should shape his/her behavior in relation to it, uniquely human. Because this sense of time and space is so deeply rooted in ToM, Scientist 03 is clearly noting that this is the difference between all NHPs and humans.

> I don't know how much imagination animals have. They have expectation and prediction. And they have, they're disappointed if they don't get what they expected but I don't think that's the same as understanding the future. Whereas our motivation, our pitfall is that we live too much in the future and not enough in the present. We're driven by these remote goals that are so much a part of our humanity that we want to achieve something and we're giving up the moment and the real true thing that we have is this moment and we're not living in the full awareness of that because our mind can very easily go: past, future, present whereas I don't think the mind of these animals work like that.

Scientist 17, who also works with macaques, agrees with Scientist 03 in regards to monkeys. For them, monkeys have, unlike humans, no ability to think of alternative worlds outside the one in which they live. Because they live in the now and are incapable of thinking about an alternative, researchers should be focused on making their lives as happy and comfortable as possible.

> The kinds of things that we're talking about involve thinking about the past and the future….So for rhesus, for macaques, for monkeys in general, I am concerned about acute distress. Am I concerned about the animals thinking about a life they did not lead? No. I don't think they have that cognitive ability.

This continual (re)construction of NHPs as lacking certain aspects of ToM, particularly those that make humans uniquely human, alleviates much of the potential guilt for the researchers' captive use of and experimentation on these animals. Because NHPs lack an understanding of time or alternative spheres, they cannot long for a different reality or some other life. This along with the argument raised by two researchers, that if these

monkeys were not being used for research, they would not even be alive,[21] is sometimes used as a justification by researchers for the continued use of these NHPs in science. Additionally, these lines of reasoning allow researchers to be primarily concerned with the comfort and immediate needs of NHPs, something all researchers using captive NHPs in this sample were adamant they are adequately doing.[22,23]

For scientists in this sample, humans, apes, and monkeys are set apart from one another based on several ToM concepts. They differ in their ability to know that another animal is thinking, to construct abstract thoughts, to understand time and space, to desire inclusion, and to have a sense of morality. They describe similarities in ape ToM to that of humans while describing fine and nuanced differences that separate the two, and further delineate these differences between humans and apes and other nonhuman primates. In so doing they carefully draw lines of similarity and difference that support the construction of (in)commesurability of various NHPs for humans. These concepts were important to scientists in describing why they use or do not use particular animals in their research and how the ways in which these concepts are understood by the scientific community and the general public influence their work.

Scientists' viewpoints about ToM in primates are mixed and somewhat contradictory, and highly influenced by the type of NHP species with which they work.

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[21] The majority of NHPs used in research labs in the United States today are captive bred.

[22] This is not to say that they do not tend to the other psychosocial needs of these animals, and indeed there are guidelines and regulations that researchers must follow in this regard (IPS 2007).

[23] The issue of how scientists feel about the captive use and manipulation of research animals, particularly NHPs, is beyond the scope of this paper. However, it is important to note that scientists in this sample described various emotions and thoughts on this topic that ranged from matter of fact and practical to deeply conflicted. Some scientists in this sample no longer conduct work with NHPs because of personal and moral conflicts with this work, while others were adamant that the benefits of research on animals for humans far outweigh the costs, and that is why they are deeply devoted to the work that they do, and to the well-being of their animals. Further, animal well-being is important for science. As Scientist 03 stated "The science is not good if they're not happy."

While all scientists in this sample believe that apes are more capable of exhibiting a ToM with regards to a greater self-awareness than other NHPs, their understanding of time, space and whether they conceive of a future or possess morality, were points of disagreement. Importantly, the ways in which scientists describe their experiences with these concepts provide a glimpse into the incredibly complex and nuanced world in which they must operate and the thoughtfulness with which they do so. In an area that is rife with substantial and critical debate, scientists in this sample display incredible openness, candor, and humility in terms of their ability to "know" the ToM of NHP subjects.

As a component of the commensuration process, ToM shapes some NHPs, namely monkeys and other non-apes, as distinctly non-human and more easily used in research. Conversely, others - namely the great apes – are constructed as very nearly human - and almost too similar to humans to be used in research. It is when these animals exhibit what are thought to be distinctly human traits that it becomes difficult to devalue them as required by the process of incommensuration. Thus apes, while on the one hand excellent proxies for humans in research as that physical "intermediate step" between monkeys and humans, when considered in a moral sense, are "just too close to us to turn around and do experiments on them"[24] (Yandell 2013). In short, ToM shows that while physical bodies may be commensurable for the purpose of scientific studies, the distinction between those animals deemed to have a thinking, feeling, and discerning mind renders some as too commensurable to be simultaneously made incommensurable

[24] This was said by Dr. Daniel Povinelli who conducts observational research among chimpanzees in a 2013 interview conducted by Science about the NIH's decision to retire the majority of its chimpanzee population. Dr. Povinelli was not contacted to be a research participant in this study.

with humans. Others, however, are similar, but just different enough, to be used in these ways.

The Sin of Anthropomorphizing

One of the key ways in which scientists engaged in anthropomorphizing NHPs, was to describe them as "child-like," "little people," or "little hairy people." As Scientist 08, 04, 03, and 11 respectively, state:

> And I've also been to different rehabilitation sites in the Congo with the bonobos and in Indonesia with baby orangutans and you know, I see little people! Little hairy people, essentially!
>
> I mean, I've seen monkeys in zoos and stuff but the first time I was face to face with a monkey, to see their facial expressions – to see their eyes and their faces, it was as if I was looking into another person.
>
> When you work with monkeys, it's extremely easy to anthropomorphize. Their eye movements are so powerful in us treating them like little people.
>
> I've also seen them act like little children with their caretakers!

The fact that these scientists see something human in NHPs when they look at them suggests that at the very core, they are acknowledging the similarities between these animals and humans. And of course, this is the basis for the study of primatology, wherein the study of primates provides a basis from which to understand important clues into human origins and evolution.[25] In describing these animals as "childlike," researchers are also unconsciously reengaging with ToM debates related to when and

[25] It is important to note that primates do not necessarily represent our historical past per se, given the fact that they are currently living now. However, studying primates using the comparative method allows us to identify selective pressures that may have contributed to who we are today and can help us identify traits that may have evolved in a distant common ancestor and that can provide important clues about our own evolution, development, and possibly even our future.

how human children develop ToM. By painting NHPs as "little children" it places them back in nebulous territory where their abilities related to TOM are again brought into question. Further, by likening these animals to children, they are, perhaps unconsciously, acknowledging these animals' vulnerability which then means they require scientists' protection and care.

Scientists in this sample noted that it was the childlike qualities of NHPs that often provided the portal through which they are able to access and engage with the more human-like qualities of these animals. This is evident in Scientist 04's description of NHPs he works with as "autistic children." Seeing them this way allows Scientist 04 to better tap into what the animals need in terms of stimulation and enrichment, and enables provision of the best care possible for them. However, Scientist 04 is quick to point out that even though the act of anthropomorphizing is beneficial to both him and the animal, it is "totally inappropriate, because they're just animals."

This need to continually draw the boundary of animals as "still" or "just" animals was pervasive throughout interviews with scientists. Despite pointing out the similarities through anthropomorphic descriptions, they clearly felt the need to demarcate them as distinctly animal and not human. Others went further to point out the dangers of anthropomorphizing, both for the lay public and scientists whose work depends on the public's ability to understand and support the use of animals in biomedical research. Scientist 17 describes an overly anthropomorphic construction of animals in movies and other media, which results in a hyper romantic and emotional view of animals. Because people are indoctrinated into these beliefs about animals at a young age, changing such (mis)perceptions is very difficult, and makes scientists' work more challenging. This is

because their work depends on their ability to clearly and distinctly draw lines between animals and humans, and for the public to be able to understand this in a scientific, non-emotional way.

> Another big factor that I think contributes, is that we're now like the third generation of Disney. What you realize is people are really informed by a lot of anthropomorphic viewpoints like Disney movies and I think have just, um, really kind of incorrect ideas about animal cognitive and emotional processes. It's a kind of magical thinking.

Anthropomorphic depictions of animals contribute to problems for scientists in this area in three key ways. First, several scientists in this sample noted that anti-animal testing advocates often use anthropomorphic depictions of animals in their campaigns to educate the public. This presents a significant problem for scientists in terms of public support for their work, and is something they must actively work to counter. Second, anthropomorphic views of animals influence the ways in which the public understands and views animals, and thus impacts what they are willing to accept in terms of research on them. Second and relatedly, anthropomorphism as propagated by Disney and other media allow animals to become commensurate for humans in the public's view through depictions of talking dogs and pigs. Just as in the case of the great apes in the ToM section above, animals viewed in this way can be seen as too similar to humans to be able to be justified for use in research, working in opposition to scientists' aims. If animals are seen as being similar to humans in ways such that the public comes to view them as undeniably possessing a ToM, as is often depicted in these movies, it can result in opposition to or decreased support for the use of animals in biomedical research among the public.

Lastly, scientists suggested that poor educational systems and a political climate of fear over the last fifteen years has led the general public to question science and the scientific method, leaving the populace with a poor understanding of science, scientific research, the need for translational research, and how to interpret findings as reported in journals or the media. Several scientists in this sample noted that because of this they no longer engage with the public, while others said that this is exactly why they engage in local activities that encourage communication between the public and scientists. It is here that they are able to talk about their work in ways that are educational and answer questions, allay fears, and respond to criticism from the media, animal rights activists, and so forth. These avenues also provide critical spaces for them to engage with the public's anthropomorphic depictions and ideas about animals. In so doing, scientists are able to clearly define animals and humans in non-emotional, scientific ways, which is crucial because if these lines and categories are fuzzy, then the processes of (in)commensuration cannot be engaged.

Other scientists, however, suggest that if utilized correctly, there may be a role for anthropomorphizing in science. In describing what Scientist 07 termed a "phobia of anthropomorphizing" in the neurosciences, Scientist 07 also points out that it may actually be what enables scientists to define what is unique to human animals and which sets them apart from nonhuman animals. Below Scientist 07 implies that as animals, humans share a great deal many traits and characteristics with other nonhuman animals. It is only through considering humans as animals that differences and similarities can be defined. Moreover, just as cultural anthropologists have shown in countless ethnographies, individuals view the world through the lens of their home or primary

culture (Lavenda and Shultz 2007) While they may be able to learn language and cultural skills to help navigate foreign terrain, the lens through which they perceive, experience, and understand the world around them is that of their culture of origin. As such, it would seem that attempting to understand animals through the lens of what it is to be human is a natural phenomenon that could, were definitions to be expanded as Scientist 07 points out, provide for a much richer and more nuanced ethological understanding of the shared traits of humans and other species.

> There's a phobia for anthropomorphism in neuroscience. So like…if you look at any of the popular psychological research people freak out if you say animals have emotion, still to this day. And it's crazy because you know there are a lot of similarities but people have been trained not to say that these things are human…or are human-like or are something that humans would do. But I think that it's partially because psychology was built on the idea that only humans had everything. You know, only humans had a mind, only humans had emotions or consciousness or anything. And we define all these things as what people have. So if they don't have exactly what we have, then it's not what they have. But if you open up the definitions, we share a lot of things. They aren't exactly the same, but they produce the same behavioral effects.

Scientist 03, in noting that humans are "just another animal," similarly calls for a more nuanced understanding of these animals, however one that is based on an understanding of their and our own separate ecologies. Like many others who reject anthropomorphizing, Scientist 03 suggests that understanding animals from a human-based perspective will lead to inappropriate and/or incorrect conclusions, and is just bad science. In this way, they are advocating for a more animal-centric and less anthropomorphic view of animals, something that they believe will be far more useful for science.

> And so why don't I treat them like little people? So many times I look at people and I find in their behavior, or in children, I find macaque behaviors and those are in the memory of our ancestors. So there are similar things that I see in macaques and humans. But you always have to understand them in their own ecology. So I don't consider them little people because I understand our behavior and I understand the context of our ecology and I understand their behavior and the context of their ecology. So I see us as just another animal.

In seeing humans as animals based on shared/common genetic, morphological, and behavioral similarities with animals, Scientist 03 points out that this is exactly how scientists and others should see animals: for what they are and in the context of their own ecology. In so doing animals are marked as distinctly non-human and incommensurate with humans. In articulating that humans and NHPs are related, but that each responds to their own particular environments and this is what shapes each into its own unique species, Scientist 03 acknowledges both similarities and differences. Through this acknowledgment they also highlight the importance of understanding that while there may be shared traits, this does not in fact make NHPs people, and therefore they should not be treated as such. While they may have similarities that are useful such that they can be considered similar enough to be used as proxies for humans in science, they are still animals and not humans, morphologically, genetically, and behaviorally different in important ways unique to that species. Scientist 03 further drives this point home by stating:

> "When I anesthetize them, I hug them, and you know it's really tough. This is the one part that I think people don't understand. They're loveable, but not the way you love your dog, or you love your family members. They're loveable in their cruelty and their nastiness of being macaques."

Thus by understanding NHPs in their own ecology, Scientist 03 is able to appreciate them for who and what they are, both their similarities and differences to humans. As such, Scientist 03 notes that they may be loveable from the perspective of a scientist who has come to understand these animals from observing and studying them in their own contexts and social worlds. However, doing so clearly demarcating them as different from other, more loveable creatures such as one's family members and pets. In demarcating NHPs in this way, Scientist 03 subtly shows how these NHPs rank in relation to other animals and humans, and intrinsically how they are imbued with a biovalue less than that of both humans and their pets. They can then be considered simultaneously physically commensurate for humans but also incommensurate, and thusly able to be used in experiments.

The anthropomorphic descriptions of NHPs by scientists are particularly significant to the work of commensuration. While on the surface they seem like simple statements about the human qualities animals exhibit, they actively describe NHPs as "having a little human in them." Or, as in the case of Scientist 03, describe humans as being "just another animal." When you reduce humans to "just another animal" it makes the use of animal bodies as proxies for human bodies, where human ones cannot be used for legal and/or ethical reasons, something that seems logical, commonsensical even.

Scientists denounce anthropomorphizing because it is antithetical to their work. For them, the divide between animals and humans, no matter how similar to humans they may be, must be clearly demarcated. As Scientist 04 stated, "monkeys and primates are animals – that's the split, that's it." When animals are kept squarely in the category of "animals" and understood in context of their own ecology as described by Scientist 03,

the shared qualities become important in terms of illuminating how animals may help us understand what makes us uniquely human.

However, it also prohibits the shared qualities between humans and animals from being blurred or overstated via anthropomorphizing of animals. This in turn makes it easier to justify animals' biovalue in relation to humans, which can then legitimize their use in science. Additionally, it enables scientists to maintain a necessary distance and separation throughout the entire research process. When these lines between animal and human are blurred, not only can it be difficult to do one's work, but it is widely believed that anthropomorphic views of animals will invalidate, or at least limit, research results.[26] Still, for some researchers, it is almost impossible not to see these animals as human in some ways, and doing so enables them to better understand and care for the animals in their charge. As noted earlier, this similarity between NHPs and humans is one of the primary reasons why primatologists, anthropologists, and others study these animals via observational studies in both captivity and the wild. These animals provide important clues about the human species, but it requires the work of commensuration in order to clearly draw the lines between what are shared traits but also those that very clearly demarcate NHPs and humans as separate.

Anthropomorphizing then has a double role in the social process of commensuration. On the one hand it serves to bring animals closer to humans so that they

[26]Additionally, anthropomorphizing animals could cause scientists to miss important clues or behavioral signs that are being exhibited. For example, if a scientist hypothesizes that camouflaged moths are more abundant in an area relative to non-camouflaged moths because the non-camouflaged moths are eaten more by their predators (i.e.birds), this could lead to a misinterpretation of data. This is because the scientist is assuming that those moths which are getting eaten less have camouflaged themselves from the birds. However, because birds see in UV light, what appears as camouflage to them is much different. Therefore, the assumption here that the moth "thinks" the bird sees one way and it adjusts its behavior to counteract this, is anthropomorphic thinking. Thus, if anthropomorphism is used, hypotheses and data to support or reject them can severely limit the scientific process.

can be better cared for while in captivity and for humans to create bonds with the animals which in turn enables them to be better research subjects. At the same time, if scientists keep their anthropormorphizing tendencies in check, it can help ensure that scientists do not misattribute human motivations to animals and obscure what the animals are actually doing, or their motivations. These are key to understanding nonhuman worlds. This importance of seeing them from within their own contexts as animals, along with the fear of committing the "sin of anthropomorphizing," however, ensures that animals are kept neatly in the category of nonhuman animals, clearly separated as incommensurate with humans. Rendering them incommensurable in this way then allows for their use and manipulation by science in ways considered unethical to treat humans. In short, these quotes illustrate that scientists' work with animals requires commensuration to happen *up to a certain degree*, and while often useful to the scientific endeavor, anthropomorphizing can often take this too far.

Discussion

This paper bears witness to those who are invisible in the process of commensuration: both those scientists meant to "do the work" of science, and those animal bodies upon which that work is done and through which knowledge is created and human lives are saved. The narratives presented here reveal a complex human reality, one intimately connected to animal lives and experiences. This work entails extensive emotional and relational work on the part of scientists in order to produce these relationships between bodies. What emerges from interviews with scientists on the topic of animals as objects of experimentation is not a uniform view of and rationalization for their use in biomedical research. Rather, interviews offered deeply nuanced narratives

largely characterized by internal conflict and emotion from scientists whose own livelihoods depend on these animals. This internal conflict often results in a multipositionality of viewpoints, or multivocality, with contradictions and sometimes confusion easily visible. For example, Scientist 05 is quoted above as stating that "humans are more valuable then animals…so why not, it makes sense to do research on something that's less valuable than humans." However, just a few minutes later, this scientist stated the exact opposite: "I'm not saying that because I'm higher value than an animal I have the right to do it. That's not what I'm saying, and I'm not treating them as less valuable." This scientist went on to reason that the "value" here has to do with the fact that these animals are highly important for science and because of that scientists go to great lengths to ensure their safety, happiness, well-being, and that they experience the least amount of pain possible in experiments. Still, comments such as this by Scientist 05 illustrate the conflicted feelings and multipositionality that scientists experience in doing this work.

This multipositionality can be further seen in Scientist 08's comments about their beliefs on whether the great apes should be used in research, which Scientist 08 adamantly opposes. However, later in the interview this scientist backtracks and notes that there are in fact times when using a great ape would be appropriate and allowable. Interestingly, this scientist also is very carefully crafting a hierarchy of animals, denoting differences between them and the great apes in terms of ToM.

> "I don't necessarily take great offense to people working with macaques and that's because I tend to think of them as 'rats of the primate world'. There are so many of them…I have no problem, no moral or ethical problems with research done on macaques or other species. But I think I would feel more strongly if the roles were reversed, if

> orangutans, bonobos, chimps or gorillas were the primary models for these biomedical tests. I think it's about the recognition of another sentient being that is really bright and to do research, you have to basically put them in jail. But if it turned out that there is a discovery next week or year that gorillas share a homologous gene that is critical for our understanding of some neurodegenerative disease like Alzheimer's or Parkinson's or cancer, I mean who wouldn't try to the best of their ability to establish a gorilla biomedical project, right? Ultimately you want to do the greater good, whatever can benefit the most individuals."

In addition to conflicted feelings about whether animals should be used in experiments, what kind of experiments, and which animals should be used, scientists often talk about their research animals in ways that show they were trying to maintain distance, despite having developed very close relationships with them. Because of this, they often described a deep respect and sometimes affection that borders on love for their research animals. In Scientist 03's description of a relationship they share with one of their macaques, we see them be very clear that they are not pets, but in actuality, the way that they talk about this animal and their role in its life as caregiver, protector, and friend, is similar to the way in which many people do talk about their pets. Scientist 03's description of the sadness, pain, and difficulty experienced when the monkey was euthanized is reminiscent of how many individuals describe the way in which they feel after a beloved pet has passed on.

> "I had a monkey here, [ ] I knew him for twelve years. That's longer than a pet. I don't consider them my pets, but it's a very intense relationship. You have to do things to this animal, but at the same time you're the guardian and the protector of this animal too… Dying is not a loss in itself, the process of dying. Not seeing them the next day and seeing the empty cage and then they're gone from our lives, that's the hard part. It's painful for me, it's (the dying part) not painful for them."

The emergence of multipositionality in these narratives suggest that scientists often struggle with holding animals in one categorical space in the same ways that others do (Herzog 2010; Joy 2010; Shir-Vertesh 2012). Scientists' descriptions illuminate how they are conflicted in their relationships with the lab animals they have come to know so well and in their ability to express themselves in relation to the work that they believe in so very deeply and which is often emotional and difficult. This multipositionality is consistent with other research that has shown how the interview itself can be used by participants as a tool to engage in the work of constructing their identities and relationships to the issue at hand (Tangaard 2009; Eaves 2015).

However, despite the multidimensional view and multipositionality exhibited by the scientists in this sample, one constant was revealed. This was the primacy of human life over all others. Even for those such as Scientist 08 above who oppose research using animals, given the choice to use animals "for the greater good" and save humans from debilitating and life-threatening diseases, the choice is clear: human life is more important. In this view, research animals are a means to an end, an end that will improve and extend human life and reduce human suffering. The fact that human beings are suffering and animals offer scientists the opportunity to reduce or eliminate that suffering is a large part of why scientists engage in this kind of work and why they have conflicted feelings about what they do. But at the heart of their work are humans, and that is what they have to keep at the forefront of their minds to be able to keep doing the difficult work. Scientist 14 was very adamant about this and it is why they encourage their students to take the time to see the human side of the diseases they are researching in

animals. It is a way for them to see the importance of the difficult work they do in the lab and to reenergize them to continue doing it.

> **"**If people do not accept the fact that these are animals for research and the ultimate goal is to help patients and move forward science, they would not be working with me. They know what it is. So….its hard! It's always hard, it is what it is. So, deal with it. That's the reason why, for example, that I make sure my students go to see the patients. So they understand why we are doing this, not because it's interesting. The reason behind this. You know, people are suffering, and when they hear a patient that says to them, oh it would be so great when you find a solution for us, or for my kids. That keeps you going to the lab when things are hard."

The importance that scientists place on saving, prolonging, and/or improving the quality of human life through improving medicine via animal research is paramount. For many, this is *the* reason they do the work they do. But many also note that their work isn't *just* about humans, that much of their work will also yield important information and scientific information that can be used to improve the lives of animals in captivity, in the wild, and through veterinary medicine.

Scientists' motivations for engaging in the work they do may be a critical component of understanding their multipositionality seen in these interviews. For example, some scientists in this sample have in the past done what they personally consider to be much more invasive work with NHPs than that with which they are currently engaged. For many of these scientists then, their lenses have shifted as they've progressed through their career. This can have a profound impact in how they view their current work in relation to that of their pasts, particularly in those cases where they are working on medicines or technologies that if successful have the potential to

immeasurably improve human lives. Importantly, even for those non-invasive scientists in this sample whose work is primarily focused on understanding NHPs in their own environments, ultimately their work is about better understanding NHPs in ways that can provide clues to our own ancestral pasts and what makes humans dinstinct from other animals. When considered from this angle, the mulitpositionality exhibited by Scientist 08 above may not seem so strange or contradictory. Therefore, examining scientists' multipositionality in relation to their backgrounds and the deeply personal and/or professional reasons that drives them to do the work that they do is an important consideration can help in understanding and framing these shifts.

While this sentiment was echoed by several scientists in this sample who felt it important to speak about their work to improve human health and human society, they were also keen to describe their efforts and desires to advance alternative methods to animal research. While some scientists in this sample lament what they view on the part of the lay public as naïve in terms of the view that animals are not necessary because science has advanced enough such that most work can now be done in cell cultures or with computer modeling, others pointed out that the need for finding alternatives has never been greater. That some NHPs can be constructed as similar but just different enough, while others are now considered too similar for research, could mean that the time is coming when other NHPs will also fall into this category. As science into the minds of non-apes continues, it is possible that scientists may find evidence of the same social lives and TOM capabilities, or at least enough for some to begin to question whether these animals should be used in research at all. Some scientists suggest that we may be moving toward a situation where the species deemed "too commensurate", i.e.

apes, will need to be replaced by the one that is "just commensurate enough," i.e. NHPs such as macaques, titi monkeys, and others. And indeed, several scientists in this sample lamented the loss of chimps in research, noting that in addition to posing a detriment to scientific advancement, it would likely increase the number of other NHPs used in research. However, it is possible that as the evidence around ToM progresses, the definition may shift and/or other NHPs will be shown to exhibit traits encompassed under the definition, rendering other NHPs even more commensurate or perhaps even too commensurate with humans to be used in research (See Drayton and Santos 2016 for a summary of a decade of work on the ToM of rhesus macaques). This would, of course, require an expansion of the dialogue on the treatment of NHPs in research and potentially decrease reliance on them in research as well. This could in turn increase the use of other animals exhibiting far fewer ToM traits such as dogs, cats, pigs, sheep, mice, and so forth.

The consequences of categorizing some NHPs as similar but different enough and others as too similar has important consequences for other animal species as well. As regulations around the use of apes become more stringent (see footnote #4), the need will be great, especially in the case of the neurosciences, for animal subjects who share at least some brain similarities with humans. But as the similar but different enough and too similar lines continue to shift, it may become impossible to use some NHPs in research at all. Without apes, the next best model is another NHP such as a macaque. As such, the numbers of these animals used in research is likely to increase, as was noted by several scientists in this sample. Thus, the consequence of apes being constructed as "too similar" to humans means that more NHPs will likely be used in this research. Thus, as

scientists continue to warn about the dangers of using animals like mice and rats in terms of poor data that do not translate well into humans (Mak et. al. 2014), the use of other animals in labs is likely to increase as well. This is currently happening in the neurosciences, but it is also happening in other fields such as HIV research, where feline immunodeficiency virus (FIV) is a useful proxy for the disease in humans. Thus, as the line for those animals deemed too similar shifts, the spaces where those that are similar, but different enough may open up opportunities for greater numbers of other animal species to be used in translational research studies.

However, increasing the use of "similar, but different enough" bodies could have important impacts on scientific data. Scientists are increasingly questioning whether or not animal models yield the important translational data needed for human studies (Mak 2014; Pound et. al. 2004; McGonigle and Ruggeri 2014; Seok et. al. 2013; Matthews 2008; Sena et. al. 2010; Perel et. al. 2007; Monnier et. al. 2016). Much of the problem is that basic research is, as noted by several scientists in this sample, most often done in mice. Mice, for a variety of reasons are not good proxies for humans, particularly in studies of certain diseases such as cancer (Mak et al. 2014); inflammatory diseases (Bolton et.al. 2012; Seok et. al. 2013), Alzheimer's disease (McGonigle 2014; Mullane and Williams 2014), strokes (O'Collins et. al. 2006), and asthama (Mullane and Williams 2014). But mice are not the only animal model with problems for translational research. Other animal models have yielded excellent data warranting further trials in additional animals or even in humans. However, many of these studies have proven to be futile in humans and some have had disastrous and even fatal results. One of the best examples of this is TGN1412, an immunomodulatory drug that was tested in both rodents and

cynomolgus and rhesus macaques before moving into Phase I clinical studies in March 2006.

All of the animal studies conducted with TGN1412 suggested that it would be safe to test in humans, and in fact, the dosage given to the NHPs in pre-clinical studies was 500 times higher than that given to the humans (Attarwala 2010). The specific NHPs used in preclinical testing were chosen because the CD28 receptors, which stimulate T cells and were the mode of action being examined in these studies, have a similar affinity for TGN1412 in these NHPs and humans (Hanke 2006). However, when the drug was administered to six male participants in a first-in-human study, all of them experienced systemic inflammatory responses, headache, nausea, diarrhea, erythema, vasodilations, and hypotension within ninety minutes of receipt of the drug (Suntharalingam et.al. 2006). All of the participants became critically ill within 16 hours with lung injury and renal failure (Suntharalingam et. al. 2006). Further complications were seen within 24 hours and two of the participants developed prolonged cardiovascular shock and acute respiratory distress, requiring intensive organ support for nearly two weeks (Suntharalingam et. al. 2006). Remarkably, all the participants survived, although today, nearly ten years later, they still suffer significant side effects from the trial and have been told they are at high risk for cancer and other diseases given that this experience weakened their immune systems (Attarwala 2010). Another study involving Fialuridine, a thymidine analog with antiviral activity against Hepatitis B virus, was tested in mice, rats, dogs, monkeys, and woodchucks at doses several hundred times higher than those given to humans in early phase clinical trials (Attarwala 2010). Unfortunately, however, five individuals died from hepatic toxicity and lactic acidosis in Phase 2 clinical trials, and

researchers have noted that none of the adverse effects in humans could have been predicted from the preclinical toxicity studies done in lab animals (McKenzie et.al. 1995; Attarwala 2010). Thus, these examples show that even those studies using NHPs for very specific similarities to humans may not result in data that are reliable for scientists to move drug testing into humans.

While several scientists in this sample, and others in the literature, have pointed out that one of the main problems with the inability of animal research to translate to humans is poor study design (Martin et. al. 2010), the reality is that much of these data are not useful in science or medicine. In fact, less than one third of the most widely cited animal research is later used in human clinical trials, and animal studies overestimate the likelihood a treatment will be effective by about 30% due to the fact that the negative results of animal studies often go unpublished (Mak et. al. 2014). Additionally, scientists have noted that laboratory animals may not be good research study participants given their lifestyle in laboratories. For example, scientists recently have suggested that the sedentary and stressful ways in which lab mice live in laboratories predisposes them to obesity, glucose intolerance, and premature death, issues which can have profound effects on the interpretation of these study results as well as translation into human studies (Martin et. al. 2010). The fact that scientists have now begun to question whether lab animals are in fact commensurate with their own species and thus good representations for use in science as well as what this means for translation of these data into humans, is something that warrants further consideration in the biomedical sciences and social studies of medicine.

In fact, given the reality of the poor translatability of animal research, scientists have begun to look at alternatives to animal testing which include epidemiologic studies, using autopsied humans, further in vitro studies, in silico computer modelling, human organs on a chip, microfluidic chips, and microdoses of drugs in humans. However, several scientists in this sample expressed concern about such alternatives, noting that in vitro studies and computer modelling would not yield the data necessary to understand the specific mechanics of how a drug works in a human *system.* While this may be true, the fact that "currently nine out of ten experimental drugs fail in clinical studies because we cannot accurately predict how they will behave in people based on laboratory and animal studies" (FDA Guidance 2006), suggests that animal studies are not necessarily producing results that are useful. This then points to the need for alternatives, of which nearly all scientists who use animals in research support the development (Speaking of Research Website 2016).

Perhaps most promising are micro-dose studies or Phase 0 studies in humans. These studies, for which the Federal Drug Administration (FDA) and European Medicines Agency have issued guidelines, test micro-doses of less than one-hundredth of a therapeutic dose in humans. Like animal studies, data from these studies will help scientists understand how the drug is distributed and metabolized in the body and whether or not it is impacting the correct molecular target (Marchetti and Schellens 2007). Such studies can provide critical data on whether or not a drug should continue in testing or be abandoned. They may also provide information on whether a drug might have applications other than those for which it is currently being targeted, given that scientists will be able to detect its effects on human organ systems.

As research into these alternatives advance, it is possible that fewer animals may be needed as proxies for humans in scientific research. However, until this becomes a reality, there is another important, and potentially very devastating consequence that may be resulting via the construction of some animals as "similar, but just different enough." This is the off-shoring of preclinical research studies using animals to nations with growing biotech industries including India, China, and Korea. This issue was highlighted by Scientist 16 who suggested that those animal rights activists who are against testing of animals in Western labs should focus their attention on this phenomena of off-shoring of preclinical research and the abuses these animals will suffer in places with little to no regulation on laboratory animal and/or lab worker welfare and safety. Indeed, as drug developers look to access the growing drug markets in China and India, they are driven to find the cheapest way to develop drugs. This often means moving the entire drug development apparatus to these nations, something that has been rapidly increasing in recent years (Ng 2009). However, there may be significant issues with offshoring these studies. These pertain not only to those issues of concern to animal welfare activists, but to consumers as well. Given the issues with lab studies that have been discussed above and problems that have been highlighted in the offshoring of human clinical trials by social scientists (Sunder Rajan 2006; Petryna 2009), the offshoring of laboratory studies using animals is an area that requires further consideration by those concerned about science as well as animal and human health and safety.

Conclusion

In interrogating the ways in which scientists talk about these issues, addressing the topics of physiology, ToM, and anthropomorphizing of animals are particularly

instructive. Examining the discussions of the physiological and anatomical aspects of animals alone, however, would lead to an almost black and white view of how scientists construct animals and humans as (in)commensurate for use in science. Therefore, disentangling how scientists negotiate their work in relation to ToM and anthropomorphizing, allows the more complex, nuanced, and emotional aspects of how scientists think about, engage with, and ultimately use animals in their work to come into view. This is instructive in that that it shows the fluidity with which scientists view various animal bodies and how these views vary depending on content, their own personal and academic backgrounds and experience with particular animals, and the contexts in which this experience occurred. Additionally, it can profoundly influence the kinds of research questions they ask. And without this simultaneous act of rendering animals (in)commensurate for humans, it would not be possible to use animal bodies in science in the ways that it is currently done. This is namely because in order to use animals that are so closely related to humans for research requires a distinction to be made between them and humans. If not, it risks opening deep wounds from the past where so-called "lesser" humans were used in research without consideration of the protections that should be afforded them. Further, it speaks to the off-shoring of clinical research to developing countries whereby the bodies of disenfranchised humans are often used to develop drugs for use by wealthy humans in the Western world.

In an era where it is increasingly difficult to use human-to-human data to generalize the ways in which a drug might affect certain populations, understanding how animal-to-human data are constructed by scientists should be an important point of consideration for scientists, doctors, patients, and regulators. Interviews for this research

illuminate a construction of animals for scientific use that is significantly impacted by the social ways in which humans both distinguish themselves from, and draw connections to, humans in relation to other animals. They demonstrate that the construction of animals, particularly NHPs, as commensurate for humans requires a flexible view of bodies that renders some as similar but just different enough such that they can be assigned a biovalue less than that of humans. In this way their bodies, although highly valued as proxies for human ones, are deemed less important, less valuable to society in comparison to humans. As such, they are rendered as not worthy of the same protections as humans and thus expendable and able to be used in research in ways that human ones could not. In other cases, however, NHPs, and in particular the great apes, are considered "too similar" to humans in ways that make it very difficult to assign a biovalue that renders them incommensurable with humans. As such, they cannot be rendered incommensurable in the same way that more distantly related NHPs and other animals can.

As data in this study have shown, the construction of lab animals as "similar, but different" and "too similar" continues to evolve. Scientists' backgrounds, experience with various animals and understandings continually push at the boundaries around which animals can and cannot be used in science and how they can be used. Others have noted how scientists "de-animalize" animals in order to engage in laboratory experiments with them (DeMello 2012) while others have noted how the demarcation of animals are "animals/not animals" facilitates lab work with animals (Shapiro 2001). This paper, however, suggests that scientists are engaged in a much more complex social construction of science via their construction of animals as either commensurate or

incommensurate for humans in biomedical research. Unlike much of the previous research on this topic which has been conducted via large surveys (Woch et. al. 2000; Lauber et. al. 2001; Miller and McGee 2001; Woch and Zang 2005), this ethnographic research captures much of the nuance and complexity inherent in the work that scientists do to render animals (in)commensurate for humans. Surveys, while able to cover a broad set of issues, often lack the depth, context, and nuance that often characterizes these issues, especially animal-human relationships (Woch et. al. 2000). Thus, the use of ethnography and attention to multivocality in the analysis of this data allows for a much richer and more robust view of the complex ways in which scientists engage in their work.

They are engaged in the very difficult work of rendering animals as not only appropriate and applicable proxies for human bodies from a scientific standpoint, but also from an ethical one. They continually define and redefine boundaries. And as these boundaries continue to be pushed and pulled, it will have significant impact on the questions that scientists can ask, how the research is conducted, the scientific research results, and what it means for medical (both animal and human) progress. These changing lines may mean that one day, no NHPs will be available for the conduct of neuroscience studies. While this may mean that greater numbers of other animals could be used, but could also change our ability to know certain things. At the same time, not being able to use the best available animal models for such studies might expand the types of questions we ask, the ways in which we ask them, and as hinted at by some – force scientists to more fully incorporate the social lives of lab animals into research questions, design, and analysis. Doing so will require scientists' continued engagement with the flexible an

nuanced ways described herein of making animal bodies (in)commensurate for human ones in science.

CHAPTER 3

Pets and the Human Microbiome: Perceptions of Dogs as Probiotic Delivery Systems

Introduction

One of the most notable scientific discoveries of the last decade has been the important roles that the hundreds of trillions (Valasquez-Manoff 2015) of micro-organisms in our guts, saliva, internal organs, and on our skin, commonly known as the microbiota, play in promoting good physical health and emotional well-being. Research on the microbiota has subsequently exploded in recent years and we now believe that it plays a key role in several key biological and physiological functions including autoimmunity (Horai et. al. 2015), cognition (Gareau 2014; Smith et.al. 2014), the blood-brain barrier function (Braniste et. al. 2014;), systemic inflammation (Forsythe 2007; Karimi et. al. 2009; Minniello et. al. 2010; Forsberg et. al. 2013; Belkaid and Segre 2014) and neuroinflammation (Lee et. al. 2011), emotional behavior (Bravo et. al. 2011; Smith et. al. 2014; Heijtza 2011), and mental health and psychiatric illnesses (Rook et.al. 2014; Haroon et. al. 2012; Miller and Raison 2015; Raison et. al. 2010; Rook et. al. 2013; Rook et. al. 2014). As a result of these scientific discoveries, the public has been inundated with messages in the media about the effects of the micriobiome on human, animal, and ecological health (Pollan 2013; NPR 2015). Additionally, the number of probiotics, products that claim to restore and/or improve the flora of one's gut, is projected to grow 7.4% annually between 2014 and 2020 (Transparency Market Research 2015). Simultaneously, in recent years there has been an exponential growth in the interest

around human-animal interactions, bonds, and the role animals play in human health. This too can be seen in the number of stories in the lay media (NPR 2012; Fields 2013), posts on social media, and the growth of pet supply and related industries (APPA 2016).

Recent research has shown that germs, dirt, and pets can be beneficial to children by reducing the incidence of immune-mediated disorders, including asthma and allergies (Yazdanbakhsh et. al. 2002; Almqvist et. al. 2003; Havstad et. al. 2011; Hanski et. al. 2012; Lynch et. al. 2014). Research has also found that married couples share more of their microbiota with their dogs than they do with their spouse (Song 2013) and that these effects are closely related to the diversity of microbes one is exposed to throughout one's life (Gereda et. al. 2000a; Gereda et. al. 2000b; Braun et. al. 2002; Gehring et. al. 2007; Gehring et. al. 2008; Douwes et. al. 2006). Such scientific discoveries connecting human, animal, and microbial health have been of interest to the general public and have been picked up by the press (Park 2012; Fang 2014). This has led many to begin thinking about the ways in which their well-being is shaped by both the micro environments within their bodies and macro environments that include those people and pets with whom they live with and are exposed to routinely.

We presently know little about how the public interprets news stories related to the microbiome and how their understanding of human-pet contact and transfer of microorganisms is influencing their behavior. In this paper, I examine the ways in which individuals use pre-existing conceptual frameworks of health and illness as lenses through which to understand the body, animals, and human-animal/environment relationships. I consider how individuals think about the microbiome in terms of lay ideas

about microbes, antibiotics and probiotics, and the cleanliness of dogs' mouths, and how this influences their interactions with domestic pet dogs.

I explore these concepts from within the context of a clinical trial conducted by an interdisciplinary team at the University of Arizona to explore the effects of introducing pet dogs into the homes of older individuals. The study, *Dogs as Probiotics to Enhance the Health and Emotional Well-Being of Elderly Adults,* (Dogs as Probiotics, for short) specifically focuses on whether the same kind of immune boosting effects seen in children living with pet dogs could be observed in older adults. We examine whether the mechanism through which this any positive changes in the older adults, including psycho-social and/or immune function, might be the result of transference of microbes between pet dogs and humans. It examines whether there is a biological basis for the physical and psycho-social improvements that humans experience with companion animals that have been reported in in the literature (for a comprehensive review of this literature see Wells 2009). As an anthropologist on this team, I used ethnographic methods to explore people's relationships to their pet dogs, their perceptions of microbial transfer between species, and how these views influenced their interactions with their pet dogs and other companion animals.

Theoretical Background

The microbiome is a relatively new concept in scientific culture, having only appeared in news articles starting in 2003 (Nerlich and Hellsten 2009). Despite having received a great deal of press both in the scientific literature and the lay media, it remains an emerging concept for the majority of Americans. What were once mostly thought of as pathogens, allergens, and vectors of disease are now known to have important and

potentially life-altering, health promoting, and life-giving properties. For most people this change in perception of microbes and bacteria requires a shift in how they think about our interactions with other humans, the environment, pets, and sources of food and medicines.

My research on public understanding of science draws upon the work of Emily Martin (Martin 1994; 1997) who describes the way in which ideas about the immune system have emerged and have been taken up in various parts of American society as a means of understanding the body, health, risk, and disease. She explores how lay people and scientists have made sense of and incorporated ideas of the body and immunity through time, noting the importance that shifts in prevailing scientific thought have played (Martin 1994). Her work illustrates how as science progresses and data and knowledge are accumulated and disseminated to the public, perceptions of this information and the ways in which it is taken up also change. Like the scientific data itself, perceptions are not static but circulate and evolve over time. They are not uni-directional from scientists to the lay public, but rather are engaged in a sort of looping process whereby they have the potential to shape not only the perceptions of the lay public but also those of the scientists and even the science itself. She notes:

> "I also wondered whether 'scientific' information just traveled out of the lab into the culture and had its effects there, period. As the research went along, I learned how often the effects of scientific information could lack the kind of closure that is often produced inside the lab. Consequently, it seemed possible that there would be many roads by which new cultural constructs of the body and health could return to transform knowledge within the laboratory itself" (Martin 1997:359).

Martin's work on the lay understanding of science also draws attention to the multiple ways one may understand the same phenomena and choose to apply different frames for understanding in different contexts. This is in line with theories of multivocality.

Multivocality (Bakhtin 1981) is a useful tool in understanding individuals' perceptions of human: pet interactions as it suggests that our utterances about a topic are best understood in the context of an exchange with other people in our lives (who are both seen and unseen). Our utterances on issues are in response to the imagined positions of others, and therefore are anticipatory in relation to what they might say. As such, our utterances are embedded in an ongoing dialogue with others, and positions they represent.[27] Multivocality can help resolve situations where there are instances of apparently contradictory "voices" within a single speaker or utterance.[28] It is particularly useful as a lens in this study given that how people feel about and interact with animals is often varied and highly reliant upon contexts, personal history and experiences.

My research is also informed by the "the many roads" concept in PUS. This concept draws attention to the tendency for scientists to dismiss lay models of the body and health as inaccurate and lacking in credibility (Wynne 1996) despite the fact that such knowledge is often based on experience and observation. Individuals are constantly engaged in making sense of the world around them using explanatory models, tools, and concepts with which they are familiar. However, because it often lacks the sophistication

[27] The dialogical self is conceived of as a dynamic multiplicity of positions in the mind, and these are in constant conversation with the utterances around them.
[28] The description here of multivocality and Bahktin are informed by personal communication (email) with Dr. Dana Osborne (4/24/16).

and language of scientific expertise, such knowledge is often derided, overlooked, and ignored by scientific experts. [29]

My work is further informed by Wagner (2007) who uses "vernacular science knowledge" to show the ways in lay expertise may not always be accurate in the eyes of scientists and can at times be problematic, but serves an important function as "acceptable and legitimate belief systems in discourses with other lay individuals." Wagner uses a variety of examples to show how these explanatory systems form useful and important ways of knowing and communicating among the general public. This is particularly useful in understanding how individuals make sense of new concepts such as the microbiome and animal-human interactions, as they struggle to incorporate statistical and scientific facts into their already existing ideas about germs, microbes, health and animals.

Methods

This study employed various ethnographic methods within a clinical trial in order to illuminate the ways in which individuals assemble ideas about human : animal : microbial connections and relationships. Ethnography is a powerful tool through which lived experiences and lay understandings not only become visible, but are taken seriously as important nodes in the social construction of science (Martin et. al. 2013).

The Dogs as Probiotics study was implemented between March and September, 2015 in Tucson, AZ. Individuals who were between the ages of 50 and 80 and who had not had a pet dog or taken an antibiotic in the preceding 6 months were eligible to

[29] For examples of this see Wynne's work on sheep herders in Cumbria (1996) as well as breast cancer screening in light of recommendations to shift age at first mammogram to 50 (Barker and Galadi 2011), AIDS research (Epstein 1995), and various detrimental effects of environmental contamination (see for example Brown 1992) and most recently the Flint, Michigan water crisis.

participate. Individuals already living with cats were not excluded from participation.[30] Of the twenty individuals who were enrolled in the study, three dropped out prior to receiving a pet dog.[31] Thus, 17 individuals completed the study which consisted of individuals selecting a pet dog through the Humane Society of Southern Arizona (HSSAZ) to foster for the duration of the three month study. Participants were given the option to adopt the animal at the end of the study.[32] Fecal, buccal, dermal, and blood samples were collected from human study participants and they participated in in-depth, semi-structured recorded interviews at four in-clinic study visits: baseline, Month 1, 2, and 3. Fecal, buccal, and dermal samples were collected from canine study participants at baseline, Month 1, 2, and 3 visits.[33] Home visits occurred at least four times during the study, once prior to the dog's arrival in the home to help participants prepare and at least three times after introduction of the dog to trouble-shoot problems and deliver study devices. Additional visits and training sessions were provided upon request by study participants.

[30] Given the lack of data on how cats affect the microbiome of humans or other animals, we elected to allow individuals who were already living with feline companion animals into the study. As this was a pilot study, researchers determined that data from these individuals may yield important and/or useful data on the microbiome of interspecies households.

[31] Two adopted dogs before baseline measures could be collected and one participant became ill and was prescribed antibiotics by her physician.

[32] Of the 14 dogs that were fostered in this study (3 couples participated and only one dog was fostered per couple), 12 dogs were adopted and two were returned into the foster care program at the HSSAZ. These two dogs were both adopted within 48 hours of return to the HSSAZ. The HSSAZ credits the study with the fast adoption of these dogs due to the "vast" amount of information fosters were able to give to the new adopters about the dogs. It is also important to note that these dogs were not adopted by their study fosters not because of any deficiencies or issues with the dogs themselves, but due to lifestyle changes/issues in the foster family itself that made it difficult for them to adopt the dog at the end of the study.

[33] Canine study participants' blood was not sampled in this study due to the invasive nature of such procedures. The Humane Society of Southern Arizona, a key partner on this study, has an explicit policy about the use of its animals for research studies. This study was subject to scrutiny by executive staff members and the HSSAZ board, all of whom approved the study given its potential to generate useful information and data that might increase shelter dog adoption worldwide. However, the study approval was granted only as long as invasive measures such as blood samples were not collected.

In-depth, semi-structured interviews with the seventeen study participants occurred at four time points in the study (baseline, M1, 2, and 3). Interviews generally lasted between thirty and forty-five minutes, were recorded, transcribed and coded for analysis using MaxQDA. Topics covered in the interviews included a brief life history at the baseline visit; knowledge and perceptions of the microbiome, probiotics, antibiotics, microbes; sources of this information and/or knowledge; use of over-the-counter or prescription probiotics and antibiotics; use of foods or substances as probiotics and/or antibiotics; prior relationships with animals; development of relationship with the foster dog; and knowledge of zoonotic illnesses and any experiences with them. In addition to gauging participants' knowledge and feelings on these issues, I was interested in understanding how they changed over time, throughout the course of the study. Further, field notes from home visits and participant observations at training sessions and the HSSAZ were typed and coded as an additional data source.

In addition to those participants who fostered a dog as part of the study, I conducted interviews with members of the general public. During the recruitment phase of this study, we received extensive media coverage in local, national, and international papers and websites, which resulted in a large number of emails and calls from potential participants and individuals interested in sharing their stories and beliefs about the health benefits of dogs for humans. These emails and phone calls provide additional rich data and context on this this topic and as such are included here (N=20) and noted throughout the paper as the "unsolicited sample."

The three themes that emerged as the main explanatory lenses participants used to talk about the topics in the interviews (i.e. the hygiene hypothesis, antibiotic paradox and

dogs' mouths as clean and healthy) arose de novo from these conversations.[34] Importantly, interviews with participants revealed paradoxes in how individuals think about and interact with pets.[35] This led me to explore how individuals are often simultaneously trying to reconcile information and experiences they have had with germs as both good and bad entities, antibiotics as live-saving medications that are also highly problematic, and how dog saliva can be a source for both positive and negative transfer of bacteria.

Results

Lens 1: Hygiene Hypothesis

One of the primary ways that individuals understand the role that microbes play in human health and disease is the hygiene hypothesis, also known as the "old friends hypothesis". This hypothesis suggests that the rise in allergies and autoimmune dysfunction may be due to the increased cleanliness and pathogen free environments (Strachan 1989). In modern life we have lost touch with many of the old microbes that we co-evolved with, and scientists believe this may be the reason why we have become more susceptible to illnesses, and why ailments like asthma and allergies are on the rise (Yazdanbakhsh 2002). This idea, termed the "old friends" hypothesis, suggests that bacteria in our bodies are remnants form our ancestral pasts. Thus, these bacteria provide and important component of our microbiomes and can provide a protective effect against

[34] It should be noted however, that because these interviews were done as part of a study described by researchers and in research materials as the "Dogs as Probiotics" study and described in the media with such titles as "The Dog Slobber Study," participants could be considered to have been "primed" to think about the topics covered in the interviews in ways that they were naturally connected to germs, microbes, and the benefits and/or dangers of dogs and their saliva.

[35] I use the term "paradox" in this paper to describe how individuals move between apparently contradictory explanatory frameworks. Use of paradoxes to explain and understand these concepts is done through semantic networks (Good 1977) whereby meaning and categories are formed as a set of symbols and experiences which generally work together for members in a society. This ensures a flexible, as opposed to fixed mode of explanation and understanding.

"bad" bacteria that may cause illness and disease in humans (Rook et. al. 2010; 2014). Findings from early studies into the validity of this hypothesis showed that children who grew up in rural areas and were exposed to close contact with animals as well as those living in larger families (Strachan 1989) experienced lower rates of asthma and other immune-mediated disorders than children living in urban areas and living without animals (Almqvist et. al. 2003; Havstad et. al. 2011; Hanski et. al. 2012; Lynch et. al. 2014). Evidence from less developed countries where children suffer less asthma and immune related illnesses also support this hypothesis, as do data showing that immigrants from developing countries to more developed nations have increased rates of these illnesses (Rottem et. al. 2005; Asher et. al. 2006). In recent years, the hygiene hypothesis has become the impetus for doctors, scientists, and public health professionals to encourage parents to allow children to have pets, play in the dirt, reduce antibiotic consumption and to take them correctly if prescribed. Additionally they have suggested that individuals increase "good" bacteria through consumption of foods rich in probiotics (Draper et. al. 2015).

When asked why they had chosen to participate in this study, individuals in both the unsolicited sample as well as in the Dogs as Probiotics study, described the hygiene hypothesis in detail, although none called it by name. Individuals described knowing that "some" germs were good for kids and that hyper-clean environments might actually do more harm than good. Anecdotes about healthy grandkids raised with dogs and sickly ones raised without were common as were descriptions of childhoods in rural areas which were less than sterile, more "germ-full" and thus "more healthy". For example, Genie[36] a

[36] All names of people and dogs have been changed.

73 year old retired nurse, when asked if she thought there might be something beneficial in terms of the transfer of germs between dogs and humans stated:

> "I think it's more than possible. I mean, I see even today that, you know, kids washing their hands – you know, with the alcohol or whatever – and they don't have an immune system anymore. So, being exposed to anything, whether it's, you know, the (dog) poop or whatever, I think it really helps."

Caroline, a 64 year old grandmother who hadn't had a dog in over twenty years, but who had them when raising her children stated it this way:

> "I mean, you're sharing the airspace with them. They're breathing the same air. You're breathing in their germs. And they're dropping their hair. I guess that's what keeps the kids from having allergies or whatever. I know we had a dog when my children were little. We always had a dog. And they had no allergies, actually they're very healthy."

And Jane, a 74 year old grandmother also noted:

> "In terms of raising young children, you don't want everything to be sterile. You know, you want them to be touching things. I see some parents just – to me, overdoing cleanliness. I mean, I never would never have thought of sterilizing my toys every night, and I know of one woman that did that. She was sort of a germaphobe."

Although none of these research participants are using scientific terminology or calling it by name, they are clearly demonstrating a command of the concepts inherent in the hygiene hypothesis. They are noting that germs, bacteria, and dirt are not necessarily bad entities, and in fact that a certain amount of exposure to these elements is beneficial to one's health, and particularly to younger individuals' health. They are all describing how exposure to things that are considered "unclean", i.e. dirt, feces, or germs can actually be healthy for individuals, particularly children. They note that the over focus on cleanliness and/or sterility, particularly when aimed at children, could actually cause

more harm than good, perhaps even render the immune system unable to mount an effective response when needed. Additionally, they are pointing out that in today's modern world, with the proliferation of antibacterial soaps and sprays, access to dirt and bacteria may not be as easy to come by as it was when they were growing up. Therefore, they suggest that exposure to positive pathogens through mechanisms such as animals are important for immune building. And as will be described further below, participants strongly believed in the beneficial bacteria and positive effects of dog saliva in particular.

Paradoxes in Narratives about the Hygiene Hypothesis and Dogs

Importantly, however, even those who described how dogs might be important to human health in terms of exposing people to immune boosting bacteria that could increase immunity and help them resist infections, individuals also described how animals could increase exposure to negative or harmful bacteria. One couple, Sally and James, 63 and 64 respectively, described on the one hand how they purposefully allowed their small dog to lick their hands when taking food to increase the chances of positive bacteria transfer, while on the other, meticulously cleaning and washing Minnie's paws after returning from excursions outside. This was done to decrease the amount of pesticides and other harmful bacteria that Minnie might pick up on the street and drag into the house on her feet. Others, like Jane, described how they knew dog kisses were good for them, but that they didn't want the dog to sit on the furniture or sleep in bed with them because they felt like this was "dirty" and could increase chances for negative bacteria transmission.

Thus, what emerges is a more complex and nuanced understanding and application of the hygiene hypothesis than might be visible if one listens to only what

people say. For when examining what people actually "do" in relation to animals, it seems that they have a stronger perception of *which* bacteria might be beneficial and where positive versus negative bacteria are found in terms of an environment or animal species host. Participants are actively engaged in working to reconcile information that they have been taught about germs and bacteria being bad for health with new information about the potential and importance of these bacteria for strengthening the body's natural abilities to fight disease and ensure a sort of homeostasis. As Martin pointed out in her work on the immune system, the prevailing paradigm for germs in the 40s and 50s was about keeping germs and bacteria out of and away from the body to protect it. As this shifted to understandings of immunity and immune building in the 60s and 70s, toward the idea that some germs might be beneficial for building and maintaining health, individuals' perceptions of this changed as well. This is important context for this study, given that the majority of study participants would have been exposed to these shifts in health paradigms and have long been engaged in making sense of it in their own understandings of health and illness. In examining how people reconcile these paradoxes, it is useful to see how ideas and concepts of health and illness have circulated in the ethos throughout their lives. Therefore, when they discuss these topics now, conversations with these previous discourses become visible and are more easily understood not as contradictions but as attempts to understand different issues at various points in time.

Lens 2: Antibiotics, Probiotics, and Dogs

Antibiotics have been hailed as the "single most important therapeutic discovery in the history of medicine" (Levy 2002; xiii). The potential of antibiotics to save lives has

meant that they have become widely used in human and veterinary medicine, plant agriculture and animal husbandry. But this wide application and use has come at a cost, namely the antibiotic paradox. The antibiotic paradox is the term used to describe the phenomena that has resulted from the overuse and misuse of antibiotics that has subsequently given rise to an epidemic of antibiotic resistant bacteria and diseases in both humans and animals worldwide (Levy 2002). Recent media stories about outbreaks of antibiotic resistant infections such as methicillin-resistant staphylococcus aureus (MRSA) and mycobacterium tuberculosis (MDR-TB) have increased public concern about these infections. Additionally, doctors and public health specialists have started to warn patients about the repercussions of antibiotic misuse and educate them about proper usage (Mayo Clinic 2016). Others have begun to call on their colleagues to reduce and restrict their prescriptions of antibiotics, while the Centers for Disease Control has even rolled out an "antibiotic stewardship" program encouraging doctors, hospitals and health care facilities to "protect patients by protecting antibiotics" (CDC 2016). However, despite these efforts, antibiotics continue to be among the most prescribed drugs worldwide (Van Boeckel et. al. 2014) and are widely used throughout the global animal agricultural sector (McEwen 2006).

And, as doctors' prescriptions of antibiotics have risen in the past decade, so have their suggestions that patients take daily probiotic supplements and/or eat foods rich in "live cultures" (Draper et. al. 2015). This comes as a result of several studies that have shown probiotics taken with or immediately following a course of antibiotics can reduce and/or eliminate antibiotic-associated diarrhea and other complications (McFarland 2006). In recent years, probiotics have come to be synonymous with pills, supplements

and foods containing live cultures that can promote digestive health. As noted above, the probiotics industry in the US is set to grow at least 7.4% annually through 2020 (Transparency Market Research 2015). The push for probiotics is not just in the field of human health, however, as these products are increasingly prescribed by veterinarians and given to agricultural animals to improve general health as well as counter issues related to the overuse of antibiotics.

Paradoxes in Describing Antibiotics and Probiotics

People in this study exhibited a high level of knowledge about probiotics, antibiotics, and the paradox of their overuse. Interestingly, when talking about antibiotic overuse, their descriptions often included the hygiene hypothesis, noting that dogs might actually be a natural antibiotic, perhaps even a probiotic, helping to combat issues related to antibiotic overuse. Participants in this study were asked to define both antibiotics and probiotics and to describe in their own words how they envision these two entities in relation to one another. In a world characterized by increasing threats from "superbug" bacteria so smart they have "outwitted" science, individuals described antibiotics in multiple ways, both positive and negative, while discussing their own fears of the implications of their overuse. Ted, a 65 year old retired accountant, described antibiotics and probiotics in this way:

> "Well, antibiotic, it's, you know, like a medicinal type of thing. It's a positive thing. An antibiotic is something medicinal to cure an illness, and probiotic is something to make you feel better without being ill. So, I don't know. It's not that they're opposed to each other. They, they're both, you know, positive – positive forces.

Ted is trying to describe a probiotic in relation to an antibiotic and wants to say that they are opposites, but knows that this is not the case given that probiotics will not make you

sick. Therefore he describes them both as beneficial and positive for human health. Below, Sam similarly describes probiotics and antibiotics in relation to one another but is careful to describe how some bacteria can be beneficial to humans and that it is important to not to eliminate them completely from the system through taking antibiotics.

> Sam: Probiotic is the opposite of antibiotic, and antibiotics get rid of bacteria, I think. And basic – yeah, antibiotic is trying to, to avoid infection. But I don't necessarily think of a probiotic as gonna cause an infection either. I know that we have, you know, I don't know how millions of different species of bacteria in your stomach – in your body, especially your stomach. We need those.

Sam describes both antibiotics and probiotics but is careful to note that probiotics are not the "opposite" of antibiotics in that they do not induce infection. His understanding of probiotics is that they have something to do with the bacteria in the stomach, but he's not sure quite how it all works. His statement suggests that he thinks that probiotics might be useful in keeping and/or strengthening the beneficial bacteria in the gut that are important for health although this isn't stated outright.

While this was common among study participants, most had a general sense that probiotics were a way to increase the good bacteria in the body. Ron perhaps explained it the best when he compared probiotics to "this stuff that recreates the beneficial bacteria that helps to break down the stuff that's in the septic system so that it'll still be working properly." Comparing probiotics to a septic system additive which can encourage positive bacteria to grow suggests a more sophisticated understanding of probiotics than other participants in this sample. For most subjects, probiotics were something generally positive, but they weren't quite sure what they were or if they should be taking them. For nearly everyone in this study, probiotics were synonymous with "yogurt." Although most people knew yogurt contains some kind of "living" bacteria, and some could even name

"acidophilus," for the most part, participants were really at a loss as to how to describe how probiotics worked on a more sophisticated scale or why they should be taking them, other than "they replenish good bacteria" or "they seem good for me."

In contrast, many participants described a love-hate relationship with antibiotics. Knowing their curative powers and importance to modern medicine, on the one hand they described them in positive terms, while on the other expressed doubts about their abilities due to an overuse that has rendered them impotent in many cases. The quote below taken from an interview with Sally and James illustrates the conflicted views many hold about antibiotics. They describe their confusion and irritation over antibiotics given to their study dog, Minnie, after her spay surgery. These antibiotics were administered by the HSSAZ staff veterinarian who suspected that Minnie may have contracted a urinary tract infection (UTI). However, given the stressful shelter environment and high likelihood of this infection, the vet did not wait for a confirmation following testing before administering Minnie antibiotics, angering both Sally and James.

> Interviewer: How would you describe an antibiotic?
>
> Sally: I hate it. I hate it.
>
> Interviewer: Why do you hate it?
>
> Sally: Because it's not good for health, and it doesn't make the infections go away at all.
>
> James: Antibiotics tend to be overused. And I think that's…That's where they get that reputation (of not working). It's probably not bad in and of itself. It just tends to be not used the way it should be used. And especially when we got Minnie, she had been on one antibiotic before she came to us (for kennel cough), but it wasn't strong enough. It didn't work. They prescribed ten days, and nada. And after that ten, she was still coughing. Then she had the (spay) surgery and they gave her more! It's just endless. Like, just using them nonstop, almost.

> Sally: Yeah, nonstop. They didn't know the result of her tests, didn't know what she had, but they already prescribed the antibiotic.
>
> James: That's right, because they thought she had a UTI.
>
> Sally: They *thought*. They *thought*! But they weren't sure. And we still don't really know if she ever did or not.

James notes that antibiotics aren't necessarily themselves bad, and in so doing acknowledges the positive aspects of these drugs. However, both James and Sally describe in clear detail the antibiotic paradox and why it has become such a grave problem for modern life. The overuse of antibiotics has rendered them ineffectual in the eyes of many. In fact, Nichter and Thompson (2006) found that this belief about the ineffectiveness of antibiotics is a major reason why many individuals today are turning to the use of dietary supplements to "prime" their immune systems so that antibiotic use isn't necessary. They also found that in those cases where antibiotics cannot be avoided, individuals use various supplements, including probiotics, in order to restore good bacteria to the gut after a course of antibiotics. This was true of several participants in this study who described adding yogurt to their diet for several days after a course of antibiotics on the advice of their doctor and/or family members and friends. Because antibiotics often affected their digestion in negative ways while helping their illnesses, yogurt consumption was used as a way to counter these effects and restore their digestion.

This was aptly described by Sam, who talked about how antibiotics "cleaned out" his system when doctors gave him several doses before, during, and after surgery. Since having the surgery a year prior, he had not once had a solid stool. However, almost

immediately following the introduction of his study dog Patches, into his home, Sam reported positive changes in his stools. Within one month of sharing his home with Patches, his normal stools had returned and he hadn't experienced any soft or liquid ones. In fact, at every visit throughout the study, Sam mentioned his improved stools, and by the end of the study was convinced that Patches had had "something" to do with this improvement.

> Sam: Before Patches came into play, I don't think ever since that surgery that I've had a real bowel movement that wasn't, you know, more closer to diarrhea than… And now I do. Now they're solid. Solid stools.

Similar to how participants engaged with ideas of germs, discussions about antibiotics revealed the work that individuals do to reconcile their ideas about the importance of antibiotics for human health but also the negative consequences that taking them can have, both at the site of the body and for society at large. They struggle with ideas of antibiotics as necessary at times of surgery or severe illness but simultaneously describe how they can make an individual sick, often through gastrointestinal problems that upset digestion and proper bowel function. They link the overuse of antibiotics with their impotence, blaming doctors who overprescribe them while hinting at the dangers of overuse for both humans and animals. Many of these study participants have taken various antibiotics throughout their lives. However, when asked at the beginning of the study when they last took one, most replied that they couldn't remember, and that they actually really try to avoid having to take them because of the way they make them feel "unwell." Individuals revealed an understanding of antibiotics as important and necessary in certain situations, but also described their disdain for them and their use in others. For these participants this was highly related to the context in which the antibiotics were

prescribed, including a desire to know whether they should be prescribed or are being done so without definitive proof of their necessity. This is evident in Janes' and Sally's description of the over medication of their dog, where they note that while antibiotics can be good and helpful in some situations this is not true for all cases, and even can be detrimental to human and animal health in the long run. These conversations also revealed the work that individuals are doing in trying to reconcile their feelings about antibiotics and somehow make them more palatable if they must take them. Many participants note that probiotics could be a way to combat the negative side of antibiotics and to ensure their own systems are kept as healthy as possible so that when/if should they ever need antibiotics, their bodies will be able to respond and the drugs will be effective.

Lens 3: "Dogs' Mouths Are Cleaner than Yours"

The idea that a dog might have a beneficial bacteria or antibiotic saliva was a theme that continually came up, both among the participants who fostered dogs in their homes and the unsolicited sample. Stories of how a dog's lick had helped cure infections and skin rashes came from as far away as Belgium and Japan, but were perhaps best summed up by John, a 69 year old retired army veteran in the Dogs as Probiotics study, when he said "A lot of people think that dogs are dirty. Bullshit, that dog and his mouth is cleaner than you are. And I truly believe that." It is important to note that this theme dominated the unsolicited correspondence, suggesting that it is a salient idea which circulates in the public discourse about the healthfulness of dogs and in particular, that their saliva has benefits for humans.

Eddie, a 70 year old local man, wrote to describe how his dog, a purebred Husky whom he had begun to call "Dr. Bailey" had completely healed a wound on his hand following surgery for basal cell carcinoma. His doctor prescribed large doses of antibiotics and suggested plastic surgery to alleviate an unsightly scar. While in the process of deciding what course of therapy and/or plastic surgery to undergo, one day Dr. Bailey demanded access to his wound. He didn't allow it at first, but because she was so persistent, it prompted him to investigate the risks of letting her lick his open wound on the internet. After conducting extensive web research on the topic of dogs licking human wounds, Eddie concluded that the risk was small and worth taking, and thus allowed Dr. Bailey access to the wound. Dr. Bailey would lick the wound several times a day for 10-15 minutes, and after about five weeks, no longer asked to lick it anymore. Six weeks later, the wound had completely and beautifully healed without an infection. Despite his doctor's protest about infection and his own initial concerns, he instead relied on his strong and deep bond with his dog, his own knowledge about wound licking among canines, and web based research to make the decision to allow Dr. Bailey to actively participate in his wound recovery. While scientists have shown that there are some beneficial bacteria in dog saliva (Hart and Powell 1990), these data remain unconfirmed in regard to positive benefits for human health. Because of this, most doctors would not prescribe or even suggest the course of action that Eddie took, especially for such an open wound. However, individuals like Eddie clearly perceive pro-health benefits of dog saliva to humans. And he is not alone. I received many such emails from people around the world eager to share their experiences with dog saliva.

For example, Jennifer, a mother of a newborn infant on the east coast of the US was concerned because of reports that have linked adverse health outcomes later in life to children born via cesarean section. Having just delivered via cesarean section, she was eager to share with me that she and her husband had been allowing their dog, a fourteen month old Wheaten Terrier, to lick the baby to encourage positive bacteria sharing as well as socialization of the baby and dog. In a unique but similar story from Australia, a father wrote to tell me about his beliefs that his son's relationship with the family dog, and in particular his mimicking of the dog's licking by licking the dog's tongue, was actually the reason his severe case of eczema had cleared.

> Zander: I have a 4 year old son, who has had eczema since he was 4 weeks old. Throughout the 4 years of his life we had discovered that he was allergic to egg, diary soy, and dust mites. His eczema was considered quite bad, where he was covered head to toe. Earlier this year we bought a puppy. At the time he also had quite severe eczema. My son's eczema went away. About a month or so after we bought the puppy, I realized that his eczema still hadn't returned. And I started to wonder with fascination if the puppy had anything to do with it. You see my 4 year old son started mimicking the puppy by licking the dogs tongue. Yes pretty gross. But I was completely fascinated. I started reading up on fecal transplants to support my wacky theory. And the more I read, the more I really believed that it was because of the puppy. We now have a 4 year old boy who is eczema free, and I am so relieved for him.

Similarly, Randall, a 72 year old living in coastal California contacted me to share his story about how his stepdaughter's "nurse dog" had licked his feet back to health from a painful rash that had persisted his entire life. After the dog licked his foot "one toe at a time from one side to the other" and did the same thing on the other foot, he felt completely comfortable for the first time in a long time. The pain had gone away, and although it would return from time to time, it was never as bad as it was prior to letting

the dog lick his feet. Additionally, he has not used Lotrimin to relieve the pain since the dog licking incident. Knowing that some people might think this odd or unbelievable, he said:

> "You know, I – it's just really hard for me to understand. Some way or another it felt like the dog knew that I had a problem, and he was able to do something about it, and he went to work and… And took care of me like a nurse, and made me feel so much better."

Although Randall's infection had been managed by an antifungal medication and not an antibiotic, what he is describing is similar to other study participants who described dog saliva as somehow beneficial and healthy for humans. Whether the saliva is an antibiotic or a probiotic, they could not necessarily discern, but to them it was clear that dog saliva sometimes works better than conventional medical treatments.

Paradoxes in Narratives about Dog Saliva

Interestingly, participants sometimes described a conflicted relationship with dog saliva, noting exactly when and where a dog should be able to lick someone. For some people, this was always, and wherever. For others, like Rosalee, a 67 year old woman from England in the unsolicited sample, dog saliva was more complex and needed to be monitored and controlled more closely. These ideas are related to not only how the saliva might help humans or be benign to their health, but also to the general uncleanliness of the dog's mouth and tongue and not "knowing where it has been."

> "If he were to lick my mouth as it were, it would be by accident. I don't actually do tongues with my dog. He does lick my face. And I have this little ritual where he licks my nose. He's allowed to lick my nose cause I feel like that's not my digestive system…I do have a belief that a dog lick is – you know. I mean, if I was hurt out when we were out walking, and he was licking my wound clean, I wouldn't be at all fazed by that, even though he licks his ass a lot."

Here Rosalee describes how she finds it acceptable for her own dog to lick her face, but not the inside of her mouth, which she believes is a direct connection to her digestive system. In prohibiting him from licking the inside of her mouth but noting that it would be acceptable for him to lick a wound on her skin, she is establishing a boundary that suggests dog saliva could be beneficial if the mode of contact is the skin. However, paradoxically she is suggesting that it could definitely be harmful if it permeated the direct connection to her digestive system, i.e. her mouth. Additionally, her comment about his "licking his ass a lot" suggests that this could be a place where his mouth would pick up bacteria to transfer to her when he licks her wounds or skin, but that is not a problem for her. Clearly Rosalee is engaged in trying to make sense of her own various understandings and complex views of dog saliva and human health and where the two intertwine. By engaging with these paradoxes, we can see that Rosalee is actively working to expand her thinking on this topic, but also has very clear, logical, and well imagined ways of understanding how dog saliva could be both positive and negative depending on how it is transferred to the body. Rosalee is engaging with an inconsistency in her own thinking but has developed a rather complex way to explaining these incongruities in her views.

Reconciling Paradoxes and Understanding Multivocality

Narratives from participants in both the dog foster sample and unsolicited sample, reveal not only attempts to reconcile complex and paradoxical views of scientific concepts and ideas, but also a nuanced multipositionality that illuminates how people can simultaneously hold views on a topic that seem in opposition to one another. This is instructive for understanding lay perceptions of the microbiome and animal-human

relations because it allows us to see how individuals think about, justify, and utilize ideas differently at different times depending on the context. It helps us to see how people make sense of these concepts and employ them variously in their own lives in ways that are neither uniform nor always consistent. In particular it is useful in this paper to examine how individuals move between various paradoxes related to hygiene and germs, antibiotics, and dogs as healthy for humans. Further, because Bahktin's work suggests that our responses are often in response to interlocutors who are not present but populate our thoughts, it provides a lens to see examine the myriad and layered concepts that play a role in lay understandings of these issues. Below I offer a few examples of the ways in which individuals in this study engage in multivocality and how this is important to understanding people's complex and varied views of the microbiome and animal-human relationships.

Maureen, a 59 year old widower, read about our study in the Phoenix newspaper and was frantic when she reached me with her cautionary story about her husband who had died of septic shock due to infection with *Capnocytophaga canimorsus. C canimorsus* is a gram negative bacteria found in the saliva of cats and dogs. While it rarely causes problems in healthy individuals, it has been known to cause severe illness and even death in individuals with compromised immune systems (Stiegler et. al. 2010). Although Maureen's husband was healthy when he succumbed to this infection, she believes it was the many years of allowing dogs to lick wounds and cuts that allowed this bacteria to enter his blood stream and lay dormant until it found just the right moment to attack his immune system.

> Maureen: My husband was a postal worker, and love, love, loved dogs. And he would let dogs lick him all the time, And I think eventually – you know, I was reading more about that bacteria (that killed him). You know, it's a real slow-growing bacteria, and I don't know if, over the years if it just accumulated in him. And he was never actually really bitten, but he did break up – our next door neighbor's dog was attacking our dog. And he broke it up, and his fingers got pretty cut up in the process. And after that, within a few weeks, he had a fever and we took him to urgent care, and within 24 hours of that incident, or that – him getting sick, you know, he had sepsis and then he had septic shock, a hospital worker called me and said, "Did your husband get bit by a dog?" And he said, "Well, this bacteria that they found in his lab work it's from saliva from a dog." And well now we're finding it's not necessarily the dog but the way his body reacted to that bacteria.

When I spoke to Maureen, she was clearly still grieving her husband's death, and told me of the anguish that she and her two adult sons experienced in deciding whether or not to keep the family's beloved dog. Having had dogs all of her life, as had her husband and their children, Maureen was torn about her choice to continue to cohabitate with a dog. On the one hand she had never even heard of anything like this happening, and was sure of the many health benefits of dogs on humans, especially the psycho-social. On the other, she was now faced with the reality that her husband, due to his own personal biology and love of dogs, had allowed him to come into contact with various bacteria, including the one that would unfortunately end his life. In the end, despite her grief, anguish, and sadness, Maureen decided to keep the family dog. She was convinced by medical professionals and her own research on this topic that her husband's death was very rare and unlikely to ever happen again, especially because it was so heavily dependent on personal biology.

Maureen's story reminds us that while dog saliva may be good for humans in some cases, in others it could be dangerous and even deadly. Her story also is an

excellent example of the multiple ways in which humans come to understand and hold their relationships with nonhuman animals. Additionally, it shows us how even within one story we can see how past experiences and conversations can become intermingled to shape complex views and positions on the same topic – in this case the relative safety of a pet dog in the home. Maureen makes sense of this by validating friends' experiences with dog saliva as positive, but cautioning that from her own experience it can also be quite damaging, depending on factors related to one's personal and health history. Canine saliva can be both positive and negative, and one may never know when, or if, that switch will happen. She reminds us that just like other medications, dog saliva and human-animal relationships are not one-size-fits-all, and that relationships with other species can put humans at risk for zoonotic infections and other diseases. Maureen's story serves as an example of how individuals make complex decisions about animals and health and wellness using a multivocality and multipositionality based on context, past experiences and conversations, and a variety of inputs from the environment. As a result, people's ways of interacting with these concepts is often fluid and can change over time.

This was the case for Ron, a 63 year old avid road cyclist who fostered a lab mix named Razzy during the study. During his first two visits in the study, he never reported any concern about the potential for transfer of harmful bacteria from his dog to him or from himself to his dog. However, during our third interview he describes how this has now shifted for him and while he is not really concerned about any immediate threats, he is now beginning to take precautions to limit the potential for bidirectional transfer of bacteria between his dog and himself.

> "Yeah, I had the thought that I wonder if it's possible to get some harmful bacteria too from the dog because – or maybe the same way from you to the dog. 'Cuz I didn't think about this before, but when I tear off pieces of that lunchmeat to give her a treat, I'm touching them. But you know, I'm not sanitizing my hands first, and so there's an avenue for me to give some of my bacteria to the dog. And now I'm also thinking you know, I'm probably gonna have to be real diligent about washing my hands thoroughly and, like, scrubbing under my nails with a little brush after I pet her, cause she's got that super, super, super fine hair and I can tell after I've petted her if I've touched my face, or you know, my hands and my arms start to get real itchy…I try not to let it happen, just because we're trained from very young age to be as antiseptic as possible.

Here we see Ron making a point about wanting to minimize the potential for transfer of bacteria given that he has been taught from an early age to be as "antiseptic" as possible. However, in all previous interviews these topics never came up. Although it is not entirely clear what has led to this change, Ron did note that having to clean up Razzy's "dust bunnies" and her fecal matter on twice daily walks had made him much more aware and conscious about the possibilities and avenues for bacterial transference between himself and Razzy. Because of this, ways of thinking about germs and cleanliness that he had been raised with, namely needing to be as "antiseptic as possible" may be re-entering his field of vision and reshaping his thinking on this topic. And yet even still, while he has become more concerned about the possibility for this transfer and engaged in ways to mitigate it, he notes that the didn't become "hyper vigilant" by refusing to let Razzy touch his fingers with her mouth or religiously washing his hands after picking up her fecal matter. Ron engaged with various sources of information on these issue in ways that reveal a multipostioned view on how to interact with Razzy. Like Maureen and others in this study, Ron's relationships and interactions with microbes, germs and animals are

filtered through attempts to both reconcile paradoxes and past experiences, conversations, and fields of knowledge to which they have been exposed throughout their lifetimes.

Discussion

This paper has placed a heavy focus on how discourses about microbes, animals, humans, past experiences and belief systems can all interact to create both biological and social experiences. Therefore, I would be remiss to point out that simply by participating in this study, participants could have been shaping scientific outcomes. Additionally, it should be noted that of the 17 participants in the study, only two had never before owned dogs. This exposure to dogs and widespread media portrayals of the study such as "The Slobber Cure," (Smith 2015), mean that study participants were likely pre-disposed to these types of positive feelings and messages about dogs and possessed a willingness to at least believe that they might have potential health benefits for humans.

As such, participants in this study likely all had some sort of belief that this is at least in part true, and therefore a worthwhile endeavor in which to participate. It is highly likely that some participants' experiences such as Sam, who had not had solid stools in over a year following surgery, were influenced by their knowledge and understanding that we as researchers were very interested in whether any physiological changes might have been taking place that participants could attribute to their new dogs. They might have been more willing to suggest such effects, much as the placebo effect in randomized, controlled, clinical trials. Expectancy effects are an issue in any clinical trial, and this one is no exception. In fact, as an open, non-randomized study, the potential for this bias may in fact be higher. However, a blinded study design would not have been feasible nor appropriate to answer our research questions.

For example, many study participants could not necessarily detail the ways in which their lives had improved since the introduction of the study dog, but they were adamant that they had, in both physiological and emotional ways. This aptly is expressed by Ted about his foster dog, Max:

> Ted: And now, with this study, I'm thinking about Max himself as being a probiotic! That in general, he makes my life better, physically and emotionally. He's pro-something!!

This was a common theme among study participants. How much study dogs were responsible, and in what ways, they could not say, but one thing was clear: every participant self- reported changes in their health, happiness, and overall well-being after acquiring the dogs. Many of the study participants also spent some time during the study considering just how transference of bacteria between themselves and the dogs might be happening. They posited that it might be both positive and negative bacteria going in both directions. Some participants, knowing they were in a study looking at these variables reported that their behavior toward their dog changed somewhat, especially in terms of allowing themselves to be licked more by the dogs. Others held strong beliefs about dog cleanliness, especially compared to other animals, and put their beliefs into action via everyday health behavior practices.

In describing the antibiotic paradox and their own conflicted feeling toward antibiotic use, participants aptly note an understanding of how overuse and misuse has spawned microbial mutation that has resulted in impotent antibiotics and a threat to humans and animals. In nearly every conversation where antibiotics were a topic,

participants described their reluctance to use these unless they were an absolute last resort. Participants noted that they felt "bad" after taking them, and had feelings that something truly important had been altered in their guts, in a harmful way. They described going to great lengths to avoid getting sick and having to take antibiotics, and in some cases, like Eddie, ignoring antibiotic prescriptions and medical advice. . For these participants, who on average were taking at least three prescription medications daily, the American norm of over-medicating is seen as something that is intrinsically changing their own biological make-up that could impact their future health and wellness. Microbes, antibiotics, and probiotics then are seen as ways in which individuals' biology are inextricably connected to both their inner and outer environments and engaged in an entanglement that can leave human, animals, and their environments altered in profound ways.

That said, this study also reveals that participants do not really understand what probiotics are, or why they should be taking them. Further, it shows that people lack information about various foods other than yogurt that can act as probiotics and how they might be able to use foods, rather than probiotic supplements, to maintain gut flora over time. Prevention using probiotic foods is wholly absent from the discussions with participants, despite the strong knowledge about yogurt as a probiotic. As such, this si a key area that scientists, doctors, and other health practitioners should begin to look at more closely in terms of how information about the microbiome and probiotics is trickling down to individuals and where improvements in communication and translatability of science to these individuals could improve.

Participants' narratives reveal models of how individual biological changes might occur because of the interconnected and looping effects of culture and our relationships with our environment, including nonhuman animals. Maureen's story of her husband's dog bite and subsequent infection reminds us that this entanglement of the biological and environmental must be considered in the context of the individual's own local biology and all of the factors that impact how different people react to different bacterial intruders. She describes her own research on the topic and her conclusion that her husband's love of dogs and interactions with them (allowing them to lick anywhere, even open wounds), led to slow changes in his biology over time. She suggests that something was brewing under his skin that when given the right set of circumstances, including biological changes in the individual, that something could one day become fatal. As such, Maureen is emphatic that interactions with pets should be cautious because they can expose us to harmful bacteria.

As Maureen's story illustrates, interviews in this study also illuminated the ways in which individuals engage with ideas of risk, related both to animals and microbes. Maureen reminds us that in a society characterized by "risk culture" (Beck 1992), individuals are responsible for their own relationship to risk. The onus is on citizens themselves to act in reflexive ways such that risk is minimized and / or negotiated. Individuals increasingly rely on a variety of information resources in order to make sense of risks and to determine the best course of action to avoid, mitigate, or live with risks. Nichter and Thompson's (2006) study on supplement use in the US, revealed how individuals assess risk in relation to their own health and wellness through "a reflexive mode of conduct whereby they attempt to negotiate and minimize risks the best they can"

(2006: 184). In their study this meant use of supplements to "boost" the immune systems to protect against illness as well as using them after a course of antibiotics to restore digestive health. Participants in this study also engaged with risk in similar ways. Individuals understand the ramifications of improper and overuse of antibiotics and actively seek ways in which to mitigate these risks. These include reducing their own use of antibiotics despite the advice of medical providers, taking supplements and vitamins to enhance the health of their immune systems. This also includes engaging with the microbial world in ways that they believe might boost their immune systems such as shunning the use of antimicrobial products, avoiding over cleanliness, and cohabitation with animals. To some extent, individuals' navigation of the risks related to antibiotic use and overuse were characterized by fear.

Although just beginning to understand the microbiome, participants' descriptions of their views on it show how new understandings of bacteria may be shaping the ways in which we interact with nonhuman actors. This study detailed many stories and anecdotes of participants increasing their close physical contact with dogs, sharing food with them, and allowing them to lick their wounds, faces, hands, and feet. Importantly, these ideas and how they are incorporated into everyday practices, is another area that should be of particular interest and concern to scientists. For example, Zander, the Australian father who is encouraging his child to lick his dog's tongue to promote bacterial transfer, is doing so based on information he has found related to fecal transfers. In his thinking around these ideas he is naturally drawing distinctions between potential sites for bacteria transfer between species – in this case the tongue and feces – and actively using this information to inform the ways in which he allows his son to interact with the family dog.

Rosalee too is doing this in her thinking around the mouth as the portal for the digestive system and thus the reasoning behind why her dog is not allowed to lick her mouth, but in contrast is allowed, and even sometimes encouraged, to lick her skin, open wounds, and nose. Examples from participants in this study illustrate that individuals are seeking out information on topics related to bacteria transfer, the microbiome, and animal-human connections, making decisions, and then employing strategies based on this information in their lives. This again offers an opportunity, and perhaps even an obligation, for scientists to ensure that data on these topics is being communicated and translated accurately to the public. Moreover, people are clearly interested in these ideas and are thinking about them constructively and creatively and drawing connections that might not be otherwise visible to the scientist so focused on the minutia of the everyday conduct of science. As such, conversations such as these offer important opportunities for an exchange of ideas between scientists and lay persons that could result in important and novel studies on both the microbiome and animal-human health relations that could move the field forward and improve animal and human health.

While it could be that participants in this study were more likely to interact more closely with their pets in order to try and "reap" some of the hypothesized benefits of the study, the mere fact that they were actively thinking about and engaging with this idea suggests that they are interacting with the "old friends" hypothesis. Like those who caution about the negative looping effects that can result from interactions between microbes, individual biology, human activity, and animal interactions, these individuals too are actively engaging with these concepts in ways that highlight their hopes that such interactions will be beneficial to both animals and humans. This study also reveals that

people often have myriad views about animals that influence the ways in which they interact with them and their willingness to incorporate new concepts such as the microbiome. Individuals' views on dogs and how we should interact with them were not uniform, nor were they always consistent within the same interview. They suggest multiple, and at times contradictory frameworks that individuals used to conceptualize, discuss, interpret, and incorporate animals into their everyday lives. As has been shown in the social science and psychological literatures, individuals' concepts about animals come from various sources and are influenced by culture, religion, personal backgrounds (i.e. family of origin, rural/urban dwelling), and so forth (Harris 1966; Rapaport 1967; Durkheim and Mauss 1963; Evans-Pritchard 1940; Geertz 1972; Leach 1964; Levi-Strauss 1963; 1969; Sahlins 1976; Valeri 2000). Individuals in this study draw upon various associations and beliefs to inform their interactions with animals that can differ depending on context, illustrating how multi-species relationships are dynamic and always in flux. Data in this paper also reveal that individuals engage in multivocality, multipositionality, and attempts to reconcile paradoxes in their own views. These data add a rich layer of context and nuance to the existing literature on these topics, which is often missed when they are examined using quantitative data collection techniques.

Conclusion

This paper explores how individuals understand a new and evolving explanatory model of the body and health, the microbiome, specifically in relation to pet dog ownership. People's views on these topics have been shaped in large part by the media, their own experiences with animals, doctors, illness, and conversations with friends and family. Further, the ways in which people think about animals, microbes, and health are

informed by a body of data on the benefits of animals for human health. This information circulates widely in the mainstream press in the form of news articles and books promoting the health benefits of animals as well as social media sites such as facebook. People have largely bought into what has been called the "pet effect" which suggests that people can improve their physical and psycho-social health and well-being, and longevity by living with animals (Allen 2003). The Dogs as Probiotics study was conducted in effort to bring more evidence-based data to bear on questions related to the role of dogs in improving human health, specifically through the mechanism of the microbiota. As such, it provides an excellent opportunity to explore how people are taking up the idea of dogs and the microbiome as emerging models of health. Drawing on Martin's work (1994; 1997) on how individuals, scientists, doctors, and the media describe and incorporate concepts of the immune system into their lives, this study looks at the circulation of ideas and flows of knowledge around germs, microbes, probiotics, and pet dogs as potential positive and negative vectors. It explores the ways in which individuals work to make sense of these concepts and incorporate them into their everyday lives, as health promotion and disease avoidance strategies. Through stories that were both joyful and devastating, people shared their experiences of how dogs and our shared microbes are involved in co-creating a new microbial self and what this means for the future of human and animal health.

Anthropologists studying how the public engages in making sense of complex scientific concepts related to the body and health have found they often do so thru the use of familiar conceptual framework (Martin 1994; 1997). This paper explores these intersections and highlights the importance of examining lay knowledge and expertise in

order to better understand how the public is engaging with these complex issues and incorporating them into their lives. The strong interest in and research on both the microbiome and human-animal relationships suggests that this work will only grow in the coming years. Therefore, the research presented in this paper, focused on understanding and utilizing lay expertise to better inform science communication and translatability to the public and, ultimately how this might inform future scientific research on these topics, is both relevant and timely. Additionally, the collection of this data within the context of a multi-species clinical trial which explores the connections between humans, animals, and their microbes provides a novel backdrop that is poised to contribute in unique ways that other explorations of these issues might not.

This is a unique multi-species ethnography given that it examines not only humans' relationships with pet dogs but also their understandings and relationships with bacteria and their own microbiota. I argue that interspecies relationships are mediated through and shaped by the circulation of information and stories available from various sources and filtered through existing lenses. These discourses are neither uniform now always consistent, morphing depending on context, timing, and in relation to past experiences, conversations, and shifting fields of knowledge. These circulating stories and discourses are shaping the ways in which individuals navigate the terrain of their own health, especially in regard to interspecies relationships. Studies such as this provide clues into the complexity and balanced ways in which animal and human health are viewed and what might be done to harness the power of these interconnections toward a better future on a multispecies level.

In using ethnography, this study also does something unique by situating lay knowledge and expertise at the center of the discussion. Scientists and medical professionals have been spending copious amounts of energy, time, and research funds on strengthening scientific data to expand the fields of microbiome science and animal-human relationships. However, this scientific knowledge does not exist only at the site of the lab or in the scientific milieu, but rather circulates and is taken up by lay people in everyday practices that can have life altering consequences. And, as this field moves forward, understanding how the public makes sense of and incorporates information related to these issues into their everyday practices should help scientists to communicate science in more constructive ways that are easily and accurately digested by the public. Moreover, and perhaps even more importantly, by listening to the public's concerns and understanding the ways in which they interpret and use scientific data, new approaches to and ideas for scientific studies are likely to emerge. In this way, science could become more of a "for the people" type of endeavor which in turn would likely increase public support for scientists and their work and encourage a more proactive public engagement with it.

Multivocality is particularly useful in understanding the ways in which people in this study move fluidly between ideas about and their relationships with animals and microbes. The paradoxes and multivocality that emerged from these conversations add a rich dimension to this data but are also an important contribution to the research in this field. This is because much of the research on how individuals feel about animals and scientific understanding is conducted via large surveys (Wolch et. al. 2000; Lauber et. al. 2001; Miller and McGee 2001; Wolch and Zang 2005). And surveys, while able to cover

a broad set of issues, lack the depth, context, and nuance that often characterizes these issues, especially animal-human relationships (Wolch et. al. 2000). Thus, the use of ethnography and attention to paradoxes and multivocality in the analysis of this data allows for a much richer and more robust view of the complex ways in which people understand and interact with these ideas in their lives.

The fact that individuals in the "unsolicited sample" actively sought out opportunities to talk with someone about their beliefs about the roles of animals in human lives and health highlights the salience of this research. This study, by examining the ways in which individuals are engaging with pet animals and the ways in which these interactions are shaping their thoughts about health, disease, and the microbiome and what this means for health, it opens up a new space for dialogue in the animal-human relationship literature. Whether grounded in scientific data or not, a vast number of people believe or want to believe that their pets have a profound impact on their health and play an important role in their personal lives. These beliefs, however, are being acted upon, as individuals engage with these concepts and employ them in their health seeking behaviors. They are doing this using their own interpretations of scientific data from the media and discussions with friends, family, neighbors and experts such as doctors. As such, it highlights the importance for the scientific community to understand lay and folk knowledge on these issues and their role in shaping behavior. While much of the data in this field has focused on the effects of pets on the psycho-social well-being of humans, this study is focused on how pets shape these ideas and how humans are actively engaged in the social construction of this scientific field of knowledge. In so doing, it highlights

the need for enhanced communicability about science to the public and thus the need for improved translational research on these topics.

As anthropologists are beginning now to shift their gaze to a re-examination of the multi-species relationship that considers the animal, human, microbial, insect, and plant worlds as important objects of study (Mullin 2002; Kirksey and Helmreich 2013; Rock et al. 2014), studies such this one will be necessary in order to provide critical data to better understand these entanglements. Studies such as the Dogs as Probiotics, by using both biological and ethnographic methods, can help move this field forward by challenging, disentangling, and problematizing the human-animal relationship. Further, by not placing one actant, human or nonhuman, as more important than the other, such studies offer an examination of the complex, dynamic, and adaptive systems in which this new nexus of multispecies relationships circulate. In these ways we may be better able to illuminate the social processes through which these actants are engaged in a continual co-construction and co-representation of one another. This is important because as Latour has pointed out, "no beings, not even human, speak on their own, but always *through something or someone else"* (2004:68, emphasis in original). Thus, examining the boundaries between animals, humans, and microbes such as in this study, enables a more full understanding of the complexity of the animal-human relationship and ultimately what it means to be human in a more than human world.

CONCLUSION

On a bright, seasonably warm Saturday morning in April, I waited as Sam, 79, and Suzie, 81, got out of their car and walked toward a wide open area with Patches, a 7 year old lab mix that they had agreed to foster for three months as part of a research study at the University of Arizona. The pilot study, *Dogs as Probiotics*, aimed to explore whether the transference of microorganisms, commonly known as the microbiota, between dogs and humans, might be *the* potential mechanism by which dogs improve the health and well-being of older humans. However, as would be the case with every single participant in the study, on this day, less than a week after Patches had gone home with Sam and Suzie, I was focused on helping them work through and troubleshoot problems that had come up almost immediately upon Patches' entry into the home. A few days before our meeting, Patches, a rather large dog who loved riding in the car, quickly jumped into the backseat of Sam's car in the garage, and as Sam tried to gently nudge him to come out, Patches turned and bit him on the hand. The bite, although superficial, caused quite a bit of bleeding, and made Suzie angry, especially given that Patches had also accidentally knocked Sam to the ground one day when excited about his walk. To Suzie, who was against Sam's participation in the study from the outset, this bite was the last straw and she wanted Patches out of their lives. As I sat with Suzie and Sam, and they talked about the events of the past week, Patches came up and put his head in Sam's lap and licked his hand where the bandage was covering the bite wound. Sam cupped Patches head in his hands and said "I love you too, boy" and a tear ran down his face. He then began to sob and I put my arm around him in an attempt to comfort him as he said, "I just can't let him go, Kim, I just can't."

We spent the next hour working with our study trainer to teach Sam and Suzie how to understand Patches' behavioral indicators a little better and how to communicate with him in a firm but loving way. We also fit them with equipment including a specific harness and lead that gave both Sam and Patches more stability, increasing their confidence and trust in one another. That weekend, the trainer and I drove to west Tucson where Sam and Suzie lived, nervous, anxious, and fully prepared to bring Patches back to the Humane Society if things were still going poorly. What we found, however, was something none of us could have imagined. Patches greeted us at the door, and with coaxing by Sam, let us into the house. Suzie looked at me and said, emphatically, "he's a totally different dog, I LOVE him!" while Sam stood by, beaming with pride. As the months wore on, Suzie and Sam would have me to their home numerous times and we would talk over a glass of ice tea about the differences Patches had made in their lives. Sam told me privately that he felt Patches was the best thing to happen to their marriage: now they had something that made them laugh every day, something to talk rather than argue about, and something that took the focus away from their difficult health issues. He also confided that having Patches allowed him to leave the house and not feel "guilty" about leaving Suzie, who was less mobile, and often stayed at home when he went out. Now, with Patches in the house, she felt "safe" when Sam was not there.

While Sam was one of the few study participants who reported feeling better in terms of their gastrointestinal health after the arrival of a foster dog into the home, nearly everyone in this study reported feeling "happier", "lighter", and like they now "had a purpose" in their everyday lives. I continue to receive emails and texts from study participants, like this one, which I received recently from Ted about his dog Max: "Max

gets better and crazier by the day. I am so grateful that he and I are together. Thank you!" While our preliminary data suggest that transference of positive bacteria between dogs and humans did not occur at the level we hypothesized, our immune data suggests an improvement in human health, and the self-reported measures about general physical and psycho-social health, suggest that dogs do indeed improve the overall health and well-being of individuals in this age range.[37]

This pilot study, while not necessarily powered to show an effect size, suggests that dogs do in fact improve the biosocial life of humans and that further research into the potential mechanisms by which this might occur is warranted. As an anthropologist whose work sits at the nexus of animal-human relations, science and technology studies, research on the "body" and clinical trials, the lessons of this study are significant for other reasons beyond measures of microbial transfer. I came to understand the importance of ethnography, empathetic listening, paying attention to multivocality and observing actors carefully in different contexts. The experience taught me that often what is left unsaid is as important as that which is explicitly stated. This is particularly true in multispecies studies. Animals, microbes and so forth cannot "speak" to us in human language, and yet the information they convey, is central to an understanding of the social worlds we cohabit.

Multi species, post human ethnographies illustrate how attempting to limit our science to randomized control trials screens out as "noise," those aspects of our lifeworld[38] that in fact makes us human and embedded in local environments. Further, the scientific method as the gold-standard of clinical science requires an objectivity that

[37] These data will be reported elsewhere.
[38] I use the phenomenological meaning of lifeworld here to point to the environmental and social background that make up one's cognitive understanding of the world and one's position in it.

rejects the idea that science is a social construction and enrolls advocates through the (re)production of knowledge by means of establishing accepted ways and means of generating and assessing evidence. We are left with a snapshot of the world that is black and white by ignoring differences that could have an important impact, constructing and then contrasting commensurable populations, and overlooking relationships not integral to research design. Overlooked are variables in our broader environment- animals, microbes, the inter-looping effects between the body and the mind as well as the animal-human binary and the animal-human-environment triangle. In this dissertation I have tried to draw attention to the ramifications of the social constructions of the human and nonhuman body in science. Further, I have highlighted our need to rethink the use of bodies as objects of scientific focus through reconfiguring the social ways with which we engage science.

Following advances in the scientific literature and a rapidly growing interest in the nonhuman other in the social sciences, I have examined the body – as human, animal, and microbial and explored the ways in which bodies are variously understood, negotiated, constructed, and produced in society, particularly when taken up as objects of study in science. The first paper in this dissertation draws attention to human bodies used as proxies for one another in transnational drug testing. It focuses on a specific type of clinical trial that has been developed to account for the idea of a Japanese bioidentity, based on Japanese ideas that Japanese bodies and brains are unique from those of all other peoples. Because of these ideas, Japanese regulatory and government officials refuse the allowance of non-Japanese bodies to be used as proxies for Japanese bodies in the generation of data for drugs to be marketed in Japan. The second paper examines the

ways in which scientists construct nonhuman primate bodies as simultaneously similar and just different enough to be able to be used as proxies for humans in biomedical research. It explores the various ways in which bodies are made to be commensurable for one another and how this impacts the science itself. In the last paper, I examine how lay individuals in the USA understand human, animal, and microbial bodies in relation to one another and in particular the salience that emerging ideas of the human microbiome have on notions of science, health, disease, and our relationships with animals and our environments.

As described in detail in the introduction to this dissertation, five themes tie these papers together: local biology and biolooping, biovalue, commensurability, and the new science of the microbiome. Local biology and biolooping are themes that run throughout all three papers, although most strongly in papers one and three. In paper one, local biology and the biolooping effects between biology, culture, history, politics, and the environment – on both a macro and micro scale - have been used to develop a sub-industry of clinical research studies for drugs intended for the Japanese market. The ways in which all of these factors are entangled in science and politics are indicative of the very real ways in which difference registers both at the site of the body and in science and the impacts it can have on both. Paper three shifts our attention from looking strictly at the ways in which local biology impacts human lives to explore the ways in which the animal-human relationship is entangled through complex interactions. Further, it examines how local biology plays a role in shaping multispecies relationships. It was beyond the scope of this paper to present data that illustrate the biolooping effects that the environment, culture, diet, exercise, and so forth are having on the microbes, animals,

humans and their interactions with one another (see footnote one above and future directions below). However, this paper offers a window into the ways in which individuals are beginning to make sense of the ideas of the microbiota, an emerging area of science, with particular attention to understandings of the interrelationsip between humans, microbes, animals, and health and disease. The paper offers a unique contribution to multispecies ethnography as an emerging field of anthropology by showing how not just two, but three species co-create one another's biological and social worlds.

In the sciences, biological material such as tissues, organs, cells and so forth, come to be imbued with a biovalue which allows them to be commodified, exchanged, bought and sold on the market. Bodies, both animal and human, have various biovalues to scientists, government officials, regulators, doctors, and patients. Papers one and two in this dissertation explore these various ways in which bodies come to be valued, how value is assigned, what this means to these various actors in the scientific nexus, and how it can affect scientific results. Biovalue of bodies is closely tied to the concept of commensurability, the idea that biological characteristics can be distilled down into relatively few key components that render whole populations of individuals as similar to one another as possible. Biovalue is key to this because it often dictates which characteristics from which populations are those chosen as variables of study populations. Additionally, biovalues of bodies are used to render some bodies as commensurable for others or incommensurable, or not equivalent. This is a key process by which scientists are able to justify the use of some nonhuman primate bodies in experiments, but not others.

I also explore the multiple and complex ways in which humans view and understand nonhuman animals and how this impacts their relationships with these creatures. In this way, the dissertation contributes to the emerging field of multispecies ethnography via papers two and three, by exploring the ways in which humans engage with animals and microbes and how these engagements impact both the construction of science and individuals' incorporation of scientific knowledge into their daily lives. Both papers focus on our relationships with animals, but in very different contexts. "Flexible Commensurabilities" uses ideas of commensurability, biovalue and multispecies relationships to explore how animals are socially constructed as acceptable proxies for humans or not, and on what this categorization is based. This paper examines a key, but often invisible and overlooked aspect of the ways in which humans experience the animal-human relationship. Diverging from the laboratory and animals in a utilitarian role at the hands of humans, paper three explores lay understandings of the emerging field of the microbiome using pet dogs and the interloping effects with human health and disease as the vehicle through which existing concepts are used to explain lay ideas of the microbiome. Unique in its structure as a three species multispecies ethnography, it also offers an opportunity from which to engage this emerging field in relation to the anthropological concept of local biology and biolooping.

Contributions to the Field

This dissertation contributes to the field of anthropology through an expansion of the use of local biology into three new avenues. These include the development of the concept of a unique Japanese bioidentity; the incorporation of local biology into scientific and anthropological explorations of the microbiome; and how local biology can be used to advance the field of health science studies on animal-human interactions. Further, this

work expands current social science work being done on the microbiome by examining it using variouis techniques and lenses from an interdisciplinary perspective. And finally, this dissertation expands the work on commensurability, taking it beyond human-human studies and into an exploration of animal : human and animal : human : microbial relationships.

With respect to Japanese bioidentity, this is a term we (Dr. Mark Nichter and I) developed to denote the concept of a unique Japanese biological identity that separates the Japanese from other peoples. This term was coined at the urging of Dr. Margaret Lock, in order to distinguish the anthropological concept of "local biologies," which recognizes "real" material difference in human populations globally but does not correspond neatly to ethnicities or national identities. "Japanese bioidentity" is an idea expressed by many (but not all) Japanese, who feel that they share a homogeneous identity, culture, and biology that is unique to only the Japanese and deeply rooted in the concept of Nihonjinron, a term used to celebrate the uniqueness of the Japanese people (Kirmayer 2002).

This dissertation applies the concept of local biology to the emerging field of the microbiome by focusing attention on biolooping effects between culture, biology, diet, human migration, human evolution, agriculture, animal-human relationships, the environment, politics, history, and socioeconomic background. It does so in a way that explores these relations as dynamic, complex, and ever mutating, not linear and static. Although scientists studying the microbiome are exploring these topics in relation to the human microbiome, often such studies are done with consideration of only one or two variables. Additionally, they have yet to fully explore the feedback loops between these

variables and their impacts on the micro and macro health of both humans, animals, and the environments in which we live, which themselves have important feedback loops to these things! As such, future papers that will describe the findings of the Dogs as Probiotics study will be attentive to these elements. I will work to open the "black box" of local biology using more complicated models that incorporate not only a complex systems approach, but that specifically explore the which bifurcation points matter and why. This is important because as has been noted throughout this dissertation, there are any given number of factors that can impact a study, but deciphering which is important and the correct ways to study its effects will be critical as this field moves forward. To be more specific, it will be important in my future work to incorporate study elements that can attend to evolution and developmental plasticity. In future papers I will continue to refine and utilize the concept of local biology as a tool enabling scientists to better incorporate a complex dynamic systems approach attentive to elements of the microbiome that are profoundly affected by human and nonhuman interactions. Further, in addition to continuing to apply and extend the use of local biology, I will explore the nuanced and fine lines that delineate differences between epigenetics and local biology. This is critical in order for this work to be taken seriously beyond medical anthropology and to be able to speak across various disciplines as I intend to do the rest of my career.

The work in this dissertation on the microbiome is important not only because it explores this emerging field from both the biocultural and medical anthropology perspectives, but because is the first study of its kind to be situated to explore what this means for animal-human interactions and species co-evolution at the biological level. The work in this dissertation explores the emerging field of the microbiome and individuals'

beliefs about this new science, how it relates to their existing understandings of health and illness, and the ways in which it impacts their relationships with pet animals. Although situated within a clinical trial aimed at looking at the biological transfer of microbes between species, this study moves beyond the biological to examine the social ways in which this emerging science is being socially constructed while simultaneously (re)shaping and constructing individuals' relationships with microbes, germs, and animals. It is more than just a case study in science and technology studies, because it asks us what this new thinking about the microbiome can teach us about how we think about the body, animals and our co-evolution and relationships to them. Through using multiple lenses and situating my work at the nexus of biocultural and medical anthropology, science and technology studies, and animal-human interaction studies, I am able to examine these issues in a much more holistic and interdisciplinary manner than can be done using the lens of just one discipline. This will be important to keep at the forefront of my work as I move forward in my career.

I would also argue that the concept of local biology has the potential to be transformative in the field of health science studies of animal-human interactions, which has to date been largely focused on animal-assisted therapies (AAT) and improvements in human psycho-social well-being. By incorporating ideas inherent in local biology, as does the study on which paper three is based, there is potential to more fully explore and characterize the biological basis behind animal-human health. Anecdotal data I collected during field work for this study suggests that doctors are currently encouraging older individuals to release their pets to shelters to avoid falls and other injuries. Others with whom I spoke are currently engaging in health seeking-behaviors that utilize their pets to

heal wounds, boost childhood immunity, and increase their own physical activity and fitness levels, even though the scientific research to support these activities is mixed (Chur-Hansen et.al. 2010; de Meer 2004; Liccardi et al. 2005; Simpson and Custovic 2005; Wells 2009; Wilson 1998). Stories I was told by a great number of individuals from all over the globe who emailed and called to talk to me about the Dogs as Probiotics study, as well as the overwhelming recruitment success we had and extensive media coverage of the project, suggest that individuals are hopeful that science will prove what they have long believed to be true about the healing power of their pets and other animals. Human-animal interaction research is poised to increase in the coming years, and bioculturally focused medical anthropologists are well positioned to play a key role in its growth and ensure that studies are scientifically robust but also attentive to the social aspects of these relationships that are so key to study outcomes.

Application of biocultural methods to explore the impacts of these relationships at the site of the body and ethnography to contextualize these data will be crucial. While biological data are useful in terms of what they can tell us about what is happening under the skin, ethnography provides an opportunity to more fully explain variables that may not make sense, be counter-intuitive and/or seem just plain "wrong." This was the case in the Dogs as Probiotics study, in which some of the psycho-social and physical activity measures seemed to tell a story that was counterintuitive to our hypothesis. For example, at the beginning of the study, participants' activity levels as measured by actigraphy and self-report increased dramatically after introduction of the study dogs. However, by the end of the study, nearly everyone in the study with the exception of one individual had reduced their activity levels rather dramatically. After talking to study participants in each clinic

interview I realized that most had stopped walking their dogs all together because of the summer heat (Tucson temperatures in mid-summer when this study was at its peak can reach upwards of 100 degrees Fahrenheit). Although some would get up earlier in the morning to walk, they would walk for less time and distance, and almost no one took evening walks. Additionally, rattlesnakes were of concern to many of the study participants, nearly all of whom lived outside of the city center. If participants did exercise with their dogs, often it would be a swim a few times a week. Recognizing that their dogs might be needing some exercise too, some would take them to dog parks. In comparing the actigraph data and self-reports to the ethnographic data, I realized that the environment was playing a large role in our study outcomes. Because physical activity can have an important effect on the microbiome (Goldenfeld et. al. 2014) it will be important to keep this ethnographic data in mind as we analyze and publish the microbiota results. Without this ethnographic data from study participants we might have been able to hypothesize about the reasons for the sharp drops in physical activity, but now we actually have those data and can use them to tell a fuller story, especially if our microbiota data are affected as a result.

This dissertation also contributes to the public understanding of science literature and highlights the importance of examining lay knowledge and expertise in order to better understand how the public is engaging with these complex issues and incorporating them into their lives. The strong interest in and research on both the microbiome and human-animal relationships suggests that this work will only grow in the coming years. Therefore, the research presented in this dissertation, particularly in paper three which is focused on understanding and utilizing lay expertise to better inform science

communication and translatability to the public and, ultimately how this might inform future scientific research on these topics, is both relevant and timely. Additionally, the collection of this data within the context of a multi-species clinical trial which explores the connections between humans, animals, and their microbes provides a novel backdrop that is poised to contribute in unique ways that other explorations of these issues might not.

Lastly, this dissertation contributes to the social construction of science literature, particularly in terms of commensurability as a lens. My research pushes the boundaries of commensurability beyond human-human clinical trials and into the realm of animal-human clinical studies as well as how individuals understand and incorporate ideas of what it is to be human through new ideas of the "microbial self." By examining commensurability via the ways in which it is used to define and justify studies conducted with animals, I am able to provide a more nuanced view of the ways in which both commensurability and incommensurability are necessary in order to define bodies as objects of scientific study. Further, by exploring how individuals are making sense of new science on the microbiome and animal-human relationships, this research is helping move commensurability into a new arena where it can be used to help describe those things that we understand make us uniquely human and those things that draw us closer to nonhuman animals. This in turn can help both scientists and lay persons understand what is potentially important about this work what it means as it is taken up in everyday practices.

The Animal Turn: Multi-dimensionality of Animal-Human Relationships

In addition to expanding the use of local biology, this dissertation also contributes to the emerging field of multispecies ethnography. In particular, it highlights the role that medical anthropology can play in this field, which has until this point been largely absent from research in this area with the exception of zoonotic diseases. Multi-species relationships have become the focus of much scientific, social science, and lay interest, especially in the last decade. In the past five years, hundreds of books have been written on animal – human bonding and relationships, animal sentience and cognition, as well as the role of animals in human life including as food, clothes, pets, tools, and even family members. Studying animals in the academy has moved well beyond the fields of animal and veterinary science. The "animal turn," as multi-species studies are often referred to, has solidified as a serious field of study, with journals and graduate programs focusing specifically on topics of animal-human interactions.

Two recently published books, both by prominent academic psychologists, attempt to untangle the often confusing multi-dimensionality of the animal-human relationship. In "Some We Love, Some We Hate, Some We Eat: Why Its' so hard to Think Straight About Animals," Herzog (2010) used examples from media to describe the various and multi-leveled relationships humans share with animals including as pets, food, family members, cockfighting, and laboratory mice. Melanie Joy, a professor of psychology and sociology, and prominent animal-rights activist, similarly writes about the ways in which we use animals in society but from the perspective of a cognitive divide that focuses on animals as pets, food, and clothing in her book "Why we Love Dogs, Eat Pigs, and Wear Cows: An Introduction into Carnism" (2010). Drawing on popular examples and written for the lay audience, these books provide a glimpse into

areas that other scholars are now taking on fully as fields of research, and that show the multi-faceted ways in which humans think about, understand, utilize, and incorporate animals into their daily lives through a complex set of values, beliefs, and understandings. However, the majority of this work today is being done in the fields of through a complex set of values, beliefs, and understandings. However, the majority of this work today is being done in the fields of psychology and sociology, fields that lack the rigorous ethnographic methodologies to actually truly interrogate the human side of the human-animal interaction. Anthropology is perfectly poised to be able to do this. Simultaneously, and as noted above, biocultural anthropology can provide the toolkit to help us untangle the nonhuman aspect of these relationships as well. Therefore, the time is now for applied medical anthropologists such as myself to engage with this field in robust, meaningful ways.

Anthropological inquiry into animals and animal-human relationships has historically focused on the materiality and functionality of these relationships and the boundaries created by humans in order to categorize animals into various spheres (Durkheim et. al. 1963; Evans-Pritchard 1940, 1956; Geertz 1972; Harris 1966; Leach 1964; Levi-Strauss 1963; 1969; Rapaport 1967; Sahlins 1976; Valeri 2000). In trying to understand the binaries and categorization into which various societies place animals, anthropologists have long cast their gaze upon those animals categorized as edible or inedible and the rituals and taboos around the preparation of certain animals as food (Valeri 2000; Herzog 2010; Joy 2010). More recently, anthropologists have begun to explore animals as pets in society (Shir-Vertesh 2012) and the ways in which we understand and incorporate these animals into our lives as more than just pets, but as

important companions and even as family members (Shir-Vertesh 2012). Noting the increasing importance that pet animals play in the lives individuals and families, especially in western societies, health researchers have begun to seriously explore the effects, positive and negative, of pet and therapy animals on individuals of all ages and with various health issues (Herzog 2011; see Wells 2009 for a review of this literature O'Hare et. al. 2015). It should be noted, however, that scientists, policy makers, and other have expressed serious concern about the designs of these studies, noting that they are often underpowered, lack a pre and post-test to discern changes due to study interventions, and lack rigorous testing methods (Herzog 2011). Given the strong interest in this area, scientists and funding institutions have begun to redesign and implement studies in order to discern whether there is an effect of animal therapy on humans. And similarly, anthropologists have begun to take note of these shifts in interests in the field of animal-human relationships such that the gaze now seems to be focusing on re-examinations of the multi-species relationship that considers the animal, human, microbial, insect, and plant worlds as important objects of study (Mullin 2002; Kirksey and Helmreich 2013; Rock et al. 2014). This new take challenges, disentangles, and problemetizes the human-animal divide and the focus on human primacy over other animals. In this process, social scientists are beginning to develop methods to better understand the ways in which these entities co-construct and co-represent one another through their interconnections. This is important because as Latour has pointed out, "no beings, not even human, speak on their own, but always *through something or someone else"* (2004:68, emphasis in original).

Additional Findings to be Published in Future

Discussions with lay persons and scientists to understand the myriad views around the use of nonhuman animals as proxies for humans in laboratory experiments, and the role of pet dogs in our lives as potential vectors for microbe transfer, revealed multivocality in ideas about various animals and their utility in human life. For example, participants routinely expressed multiple and seemingly inconsistent views about animals when asked about differences between cats and dogs, including even those participants who had pet cats before starting the study. They described cats as a potential source of infection and definitely not an animal that should be allowed to lick one regularly. This was true even of those seven participants who owned cats before coming into the study. Participants describe cats as "dangerous" while simultaneously describing dogs as "like humans" and because of their close similarities to humans, are not an animal that needs to be feared - especially in terms of germs and bacteria. And yet even though participants described cats as being potentially dangerous and not good for human health, they continue to allow them to live in their homes. To the study participants, dogs, because of their "human-like" qualities and intimate relationships with humans, are uniquely situated to provide health benefits for humans, benefits that other animals cannot offer. These feelings of dogs as human-like and as carriers/transmitters of health and well-being to humans, in contrast to cats as dangerous and disease-laden, points to an exceptionalism of dogs in (some) human societies.

In the nonhuman primates in biomedical research study, often participants would one moment speak of their beliefs in the importance of treating animals well, respecting their lives, and not keeping them in unnatural conditions for human benefit, while in the next describing their regular consumption of animal products. Often they would qualify

this by saying “Oh, but I only eat free-range chicken, or grass fed beef, or drink milk from “happy cows,” suggesting that they do have some kind of understanding that animals raised for industrial agriculture are living in the very “unnatural” conditions that they believe are so wrong for lab animals. When pushed on this further, often it would come out that with lab animals they were talking about nonhuman primates who they believe have strong similarities to humans and thus should be treated better than animals lower on the food chain such as chickens, pigs, cattle, etc. Their descriptions emphasized the ways in which animals can occupy one category in one moment and an entirely different category in the next. A hierarchy of animals definitely was evident in discussions with people throughout this study. Additionally, familiarity and proximity to various animals did play a role in individuals’ views on how certain animals should be treated. For example, people raised on farms tended to have a more utilitarian view of animals, while those with some exposure to primates felt very strongly about how NHPs should be housed and cared for, and the types of research in which they should be allowed to participate, depending on the species. Interestingly, even the most adamant dog lovers, when pressed, would agree that research using dogs was acceptable if it could benefit humans, but not one person in this study would have allowed their own dog to be used in research, even if it could save the lives of other dogs. The fixed categories for animals that have been described by anthropologists elsewhere (Valeri 2000) were nearly non-existent in this sample. Nearly all animals discussed during the course of this research, with notable exceptions such as snakes, lizards, and fish, flowed in the imaginations of individuals between categorical spaces of pets, food, and laboratory experiments. By exploring these views more closely, and examining the reasoning

between the shifting categories, a much more complex and nuanced understanding of human relationships with animals is illuminated. This is important, particularly in understanding individuals' beliefs around the use of animals in biomedical research, because to date the majority of social science research examining this topic has been done by large surveys, where context, texture, and nuance are unable to come to relief. The interviews I undertook as a part of this research highlight the need for ethnography to allow individuals to move between categories and justify their beliefs as they switch positions and voices depending on context.

Future Directions

Papers two and three of this dissertation are on based on larger projects. As such, there is a great deal that has been left out of this dissertation and which will form the basis of several future papers. In particular, from the study of the lay public's and scientists' views on the use of nonhuman primates in biomedical research, I intend to write at least three additional papers. Similar to the paper presented here on scientists' views and construction of NHPs as objects of scientific experimentation, I will look at how the general public understands, negotiates and contests their use in science. Interestingly, both scientist and lay persons described similar views and ideas about the ways in which primates live in captive enclosures in laboratory settings. As such, I plan to write a paper describing these "imagined" views of the lives of captively held nonhuman primates, how this differs from reality, and the role that this plays in people's feelings on the topic of NHPs' use in science.

Another paper currently in progress is titled: *Out of Sight, Out of Mind: The Invisibility of Animals in Agriculture and Laboratory Science and the Unwitting Role of the Animal*

Rights Movement. In interviews about animals in biomedical research, scientists and lay persons spontaneously connected the worlds of lab and agricultural animals. Noting a lack of available, credible information about both industries, they described their own intentional ignorance and how scientists and agriculturalists benefit. Participants suggested successes of the animal rights movement have silenced scientists and agriculturalists and protected them via legislation equating animal activism with terrorism. This paper will explore scientist and lay perspectives on the role of animal activism in constructing these industries as invisible, thus increasing apathy and avoidance among the public about the use of animals in them. I also plan to write a final paper from this work that reports on the use of a card-sort exercise conducted as a part of this research with the lay public. It will help illuminate much more fully on the concept of the multi-dimensionality of human views on animals and how people construct nonhuman animals as similar and/or different to human animals, with specific focus on both physiological and social characteristics.

With regard to the scientific findings related to the microbiome, immune functioning, and psycho-social measures in the Dogs as Probiotics study, these data will be published in the coming year. I also plan to write a field methods article on how to incorporate multispecies ethnography into a clinical trial of animal-human interaction clinical research. Lastly, I plan to write an article comparing the different relationships that Americans have with cats and dogs, with particular respect to people's perceptions of them as vectors of either health or disease and as pets.

In addition to these papers I have developed a plan of research for the next several years to conduct during my post-doc appointment at the University of Wisconsin-

Madison's School of Human Ecology (SoHe). SoHE has a strong emphasis on child development from ages 0-5, and has a state-of-the-art preschool facility housed inside the SoHE building on UW's campus. Some data from early childhood and school-based interventions have suggested that incorporating an animal into the classroom can have beneficial effects on children's ability to learn (Kotrschal and Ortbauer 2003). However, very little of these data have looked at intersections between why children might be learning better in the presence of a dog and whether the dog is having any biological effects on children that are in turn modifying psycho-social well-being or the ability to learn, or mediating other health effects. Therefore, I am currently planning a study that will examine the effects of a classroom dog on children in a preschool that involves a control school that will not receive the dog as an intervention. Various biological measures, psycho-social assessments, and observations will be made over the course of a year to assess biosocial changes that are occurring in these children.

Additionally, I am planning to design a study that will look at the differences in effects of farm animal-based therapy vs. domestic animal-based therapies. As has been noted throughout this dissertation, the majority of data on the effects of AAT on human health is currently problematic for a variety of reasons (Herzog 2011). Although AAT programs abound at various healthcare and other facilities nationwide, many people are calling for robust studies to discern the true benefits of these therapies (Wells 2009; Herzog 2011). Given data in this field related to biological outcome measures as cited in the introduction of this dissertation, I do not believe that these therapies have psycho-social benefits alone. This study with therefore examine whether there might be a deeper, more meaningful change happening at the site of the body that has looping effects with

the mind and is occurring via the complex adaptive relationships between human, nonhuman and environment. This study will be a comparison between a current farm sanctuary therapy program that utilizes rehabilitated farm animals to treat trauma in individuals, with a therapy program that uses domestic dogs for the same purpose. I am interested in this question because some data suggest that familiarity with the therapy animal facilitates therapeutic benefits (Shuelke 1991), whereas other data that show the benefits of farm animals on allergies and immunity suggest that these animals have a strong mediating potential for illness (Almqvist 2003). Being able to decipher what is actually having an effect on which individuals and why will be a very strong benefit to the field of animal-health research. I will again employ various biological measures, psycho-social questionnaires, as well as ethnographic methods such as observations, interviews, and so forth.

Additionally, I plan to continue to work with laboratory animals, in particular NHPs, and study their use in biomedical research. The University of Wisconsin has a premier primate testing facility along with strong activist communities who both support and oppose the use of NHPs in biomedical research. Being in close proximity to these resources, I hope to present my work on this topic at various forums throughout Madison and work with scientists, technicians, veterinarians, activists, and lay persons to continue to expand my work in this area. I am hopeful that the training I have received in being an empathetic witness will allow me to examine all facets of this field and bring evidence-based data to the table that will result in a dialogue between stakeholders on this issue, something that is more than overdue.

Conclusion

With this study and the two described above, I am laying the groundwork for a career focused on utilizing biocultural methods to bring rigorous, robust scientific data to the field of animal-human interaction studies, something that is greatly needed. My training as a biocultural and applied medical anthropologist at the University of Arizona has prepared me well for these endeavors, but I also know that learning is a life-long process. I am therefore excited to be joining a group of talented and dedicated colleagues at UW-Madison where I will have the opportunity to not only contribute positively to the growth and development of SoHE, but also continue my own development as an engaged anthropologist.

REFERENCES CITED

Allen, Karen
2003 Are Pets a healthy Pleasure? The Influence of Pets on Blood Pressure. Current Directions in Psychological Science 12 (6): 236-239.

Almqvist, C., with A.-C. Egmar, G. Hedlin, M. Lundqvist, S. L. Nordvall, G. Pershagen, M. Svartengren, M. van Hage-Hamsten, and M. Wickman
2003 Direct and Indirect Exposure to Pets - of Risk Sensitization and Ssthma at 4 years in a Birth Cohort. Clinical & Experimental Allergy 33 (9): 1190-1197.

Anonymous
2001 Genes, Drugs and Race. Nature Genetics, 29(3), 239-40.

Altevogt, Bruce M. with Diana E. Pankevich, Marilee K. Shelton-Davenport, and Jeffrey P. Kahn, eds.
2011 Chimpanzees in Biomedical and Behavioral Research Assessing the Necessity. Washington, D.C.: National Academies Press. ProQuest e-book collection: http://public.eblib.com/choice/publicfullrecord.aspx?p=3378939 accessed April 29, 2016.

American Pet Products Association (APPA).
2016 Pet Industry Market Size and Ownership Statistics. http://www.americanpetproducts.org/press_industrytrends.asp Accessed May 1, 2015.

Asher, M. Innes with Stephen Montefort, Bengt Björkstén, Christopher KW Lai, David P. Strachan, Stephan K. Weiland, Hywel Williams, and ISAAC Phase Three Study Group
2006 Worldwide Time Trends in the Prevalence of Symptoms of Asthma, Allergic Rhinoconjunctivitis, and Eczema in Childhood: ISAAC Phases One and Three repeat Multicountry Cross-sectional Surveys. The Lancet 368, no. 9537: 733-743.

Attarwala, H.
2010 TGN1412: From Discovery to Disaster. Journal of Young Pharmacists: 2 (3): 332-6.

Bakhtin, M.M.
1981 The Dialogic Imagination: Four Essays. Trans. Caryl Emerson, Micahel Holquist, ed. Austin: University of Texas Press. Pp. 249-422.

Bankoff, Richard J. with Heritiana D. D. Randrianatoandro, and George H. Perry
2015 Primate Conservation Genomics and Paleogenomics. American Anthropologist 117 (4): 742-743.

Barker, Kristin K., and Tasha R. Galardi
2011 Dead by 50: Lay expertise and Breast Cancer Screening. Social Science & Medicine. 72 (8): 1351-1358.

Bekoff, Marc
2007 The Emotional Lives of Animals: A Leading Scientist Explores Animal Joy, Sorrow, and
Empathy--and Why They Matter. Novato, Calif: New World Library.

Belkaid, Yasmine and Julia A. Segre
2014 Dialogue Between Skin Microbiota and Immunity. Science. 2014;346(6212):954–9.

Benet, L., Kroetz, D., & Sheiner, L. (1996). The Dynamics of Drug Absorption, Distribution and Elimination. In J. Hardman & L. Limbird, eEds., Goodman and Gilman's The Pharmacologic Basis of Therapeutics. (9th ed., pp. 3-28). New York, NY: McGraw-Hill.

Bentley, S.
1997 Clinical Research and CROs in Japan. Applied Clinical Trials, 6(4), 30 - 35.

Benezra, Amber with Joseph DeStefano and Jeffrey I. Gordon
2012 Anthropology of Microbes. Proceedings of the National Academy of Sciences of the
United States of America 109(17):6378-638.

Bolton, S., with D. Hassall, D. Hildebrand, W. Bruck, J. K. Huang, S. Pluchino, T. McKevitt, et al.
2012 Anti-Inflammatory Disease Therapies: Challenges and Strategies in Drug Development.
Toxicologic Pathology 40 (1): 122–25.

Braniste, Viorica with Maha Al-Asmakh, Czeslawa Kowal, Farhana Anuar, Afrouz Abbaspour, et. al.
2014 The Gut Microbiota influences Blood-brain barrier permeability in mice. Science Translational Medicine 6:263.

Braun-Fahrlander, Charlott with Josef Riedler, Udo Herz , Waltraud Eder, Marco Waser, Leticia Grize et al.
2002 Environmental Exposure to Endotoxin and its Relation to Asthama in School-age Children. New England Journal of Medicine 347:869-77.

Bravo, Javier A. with Paul Forsythe, Marianne V. Chew, Emily Escaravage, Helene M. Savignac, Timothy G. Dinan, et al.
2011 Ingestion of Lactobacillus Strain Regulates Emotional Behavior and Central GABA Receptor Expression in a Mouse via the Vagus Nerve. Proceeding of the National Academy of Sciences 108(38):16050–5.

Brotherton, P. Sean and Vinh-Kim Nguyen
2013 Revisiting Local Biology in the Era of Global Health. Medical Anthropology 32 (4): 287-90.

Brown P.
1992 Popular Epidemiology and Toxic Waste Contamination: Lay and Professional Ways of Knowing. Journal of Health and Social Behavior. 33 (3): 267-81.

Butler, Judith
Butler, Judith
1993 Bodies that Matter: on the Discursive Limits of "Sex." New York: Routledge.

Byrne, Richard W. and Lucy A. Bates
2010 Primate Social Cognition: Uniquely Primate, Uniquely Social, or Just Unique?. Neuron, 65, 815–830

Call, Josep
2007 Past and Present Challenges in Theory of Mind Research in Nonhuman Primates. Progress in Brain Research 164:35–341.

Callon, Michel
1986 Some Elements of a Sociology of Translation: Domestication of the Scallops and the Fishermen of St. Brieuc Bay. *In* Power, Action and Belief: A New Sociology of
Knowledge? John Law, ed. Pp. 196–233. London: Routledge and Kegan Paul.
Carsten, Janet, ed.
2000 Cultures of Relatedness: New Approaches to the Study of Kinship. Cambridge: Cambridge University Press.

Centers for Disease Control and Prevention (CDC)
2016 Core Elements of Hospital Antibiotic Stewardship Programs.
http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html
Accessed May 1, 2016.

Center for Drug Evaluation and Research (CDER)
1998 The CDER Handbook.
http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM198415.pdf Accessed April 9th, 2016.

Chur-Hansen Anna with Cindy Stern, and Helen Winefield
2010 "Gaps in the Evidence About Companion Animals and Human Health: Some Suggestions for Progress". International Journal of Evidence-Based Healthcare 8 (3): 140-6.

Collins, Francis S. and Lawrence A. Tabak
2014 Policy: NIH Plans to Enhance Reproducibility. Nature 505, 612–613.

Conn, P. Michael, and James V. Parker
2008 The Animal Research War. New York: Palgrave Macmillan.

Clayton, Janine A. and Francis S. Collins
2014 NIH to Balance Sex in Cell and Animal Studies. Nature 509 (7500): 282-283.

Dean, Mitchell
1999 Basic Concepts and Themes. Governmentality: Power and Rule in Modern Society Pp. 9-39. London: Sage Publications.

Dreyfus, Hubert. L. and Paul Rabinow
1983 From the Repressive Hypothesis to Biopower. Michel Foucault: Beyond Structuralism and Hermeneutics 2nd ed., Pp. 126-142. Chicago: University of Chicago Press.

De Filippo, Carlotta and Kieran M. Tuohy
2015 A Nutritional Anthropology of the Human Gut Microbiota. *In*: Diet-Microbe Interactions in the Gut: Effects on Human Health and Disease. Kierean Tuohy and Daiele Del Rio, eds. New York: Elsevier Academic Press. Pp. 17-26.

de Meer, Gea with Brett G. Toelle, Kitty Ng, Euan Tovey, and Guy B. Marks
2004 "Presence and Timing of Cat ownership by Age 18 and the Effect on Atopy and Asthma at age 28. Journal of Allergy and Clinical Immunology. 113 (3): 433-438.

DeMello, Margo
2012 Animals and Society: An Introduction to Human-Animal Studies. New York: New York University Press.

de Waal, Frans, B. M.
1996 Good Natured: The Origins of Right and Wrong in Humans and OtherA. Cambridge, Mass: Harvard University Press.
1997 Are We in Anthropodenial? Discover 18(7): 50-53.

Disotell, Todd R.
2003 Discovering Human history From Stomach Bacteria. Genome Biology 4:213.1–213.4.

Dominguez-Bello, Maria Gloria and Martin J. Blaser
2011 The Human Microbiota as a Marker for Migrations of Individuals and Populations Annual Review of Anthropology 40: 451-474

Dong, Jia-Yi and Li-Qiang Qin
2011 Soy Isoflavones Consumption and Risk of Breast Cancer Incidence or Recurrence: A Meta-analysis of Prospective Studies. Breast Cancer Research and Treatment 125 (2): 315-323.

Douglass, Mary
1966 Purity and Danger, an Analysis of Concepts of Pollution and Taboo. New York: Frederick A. Praeger.

Douwes, Jeroen with Rob van Strien, Gert Doekes, Jet Smit, Marjan Kerkhof, Jorrit Gerritsen, et al.
2006 Does Early Indoor Microbial Exposure Reduce the Risk of Asthma? The Prevention and Incidence of Asthma and Mite Allergy birth cohort study. Journal of Allergy and Clinical Immunology 117:1067-73.

Draper, Karen with Catherine Ley, Randall Staffor, and Julie Parsonnet
2015 Probiotic Prescriptions in the United States 2009-2015. Poster Presented at ID Week, San Diego, October 10.

Drayton, Lindsey A. and Laurie R. Santos
2016 A Decade of Theory of Mind Research on Cayo Santiago: Insights Into Rhesus Macaque Social Cognition. American Journal of Primatology 78 (1): 106-116.

Durkheim, Émile, Marcel Mauss, and Rodney Needham
1963 Primitive Classification. Chicago: University of Chicago Press.

Emery, Nathan and Nicola Clayton
2004 The Mentality of Crows: Convergent Evolution of Intelligence in Corvids and Apes. Science 306: 1903-1907.

Eaves, Emery R., with Mark Nichter, Cheryl Ritenbaugh, Elizabeth Sutherland, and Samuel F. Dworkin
2015 Works of Illness and the Challenges of Social Risk and the Specter of Pain in the Lived
Experience of TMD. Medical Anthropology Quarterly 29 (2): 157-77.

Epstein, Steven
1995 The Construction of Lay Expertise: AIDS Activism and the Forging of Credibility in the Reform of Clinical Trials. Science, Technology, & Human Values 20 (4): 408-437.
2007 Inclusion the Politics of Difference in Medical Research. Chicago: University of Chicago
Press.

Espeland, Wendy Nelson, and Mitchell L. Stevens
1998 Commensuration as a Social Process. Annual Review of Sociology 24: 313-343.

Evans-Pritchard, E.E.
1940 The Nuer: A Description of the Modes of Livelihood and Political Institutions of a Nilotic People. Oxford: Clarendon Press.

Fabian, Johannes
1990 Presence and Representation: The Other and Anthropological Writing. Critical Inquiry
16 Pp. 753-772.

Fang, Janet
2014 Early Exposure to Pets, Dirt and Germs are Good for Babies. IFL Science, June 9th, 2014. http://www.iflscience.com/health-and-medicine/early-exposure-pets-dirt-germs-are-good-babies Accessed May 1, 2016.

Farmer, Paul
1997 Social Scientists and the New Tuberculosis. Social Science and Medicine 44:347–358.

Fields, Lisa
2013 Six Ways Pets Can Improve Your Health. October 24th, 2013. http://www.webmd.com/hypertension-high-blood-pressure/features/6-ways-pets-improve-your-health Accessed May 1, 2015.

Food and Drug Administration (US)
2006 FDA Issues Advice to Make Earliest Stages of Clinical Drug Development More Efficient. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108576.htm Accessed April 30th, 2016.

Fleur, Nicholas
2015 U.S. Will Call All Chimps "Endangered". New York Times: June 12th, 2015. http://www.nytimes.com/2015/06/13/science/chimpanzees-endangered-fish-and-wildlife-service.html?_r=0 Accessed January 9th, 2016.

Flynn, Mark.
1999 Family Environment, Stress, and Health During Childhood. *In* Hormones,H, and Behavior: A Socio-ecological and Lifespan Perspective. Panter-Brick, C. and C.M. Worthman, eds. Pp. *105-130.* Cambridge: University Press.

Forsberg, Anna with Thomas Abrahamsson, B. Bjorksten and Maria Jenmalm
2013 Pre- and Post-natal Lactobacillus Reuteri Supplementation Decreases Allergen Responsiveness in Infancy. Clinical Experimental Allergy 43(4):434–42.

Forsythe, Paul with Mark Inman and John Bienenstock
2007 Oral Treatment with Live Lactobacillus Reuteri Inhibits the Allergic Airway Response in Mice. American Journal of Respiratory and Critical Care Medicine 175(6):561–9.

Foucault, Michel

1990 Power as Knowledge. *In* The History of Sexuality. R. Hurley, ed.,Pp. 518-523. New York: Vintage Books.

Franconi, F.with Sandra Brunelleschi , Luca Steardo, and V. Cuomo.
2007 Gender Differences in Drug Responses. Pharmacological Research 55:81–95.

Gareau, Melanie G.
2014 Microbiota-Gut-Brain Axis and Cognitive Function. *In:* Microbial Endocrinology: The Microbiota-Gut-Brain Axis in Health and Disease. Lyte, Mark and John F. Cryan, eds. Pp. 357–71.

Gastaldo, Denise
1997 Is Health Education Good for You? Re-thinking Health Education Through the Concept of Biopower. In A. R. Peters & R. Bunton, eds., Foucault, Health, and Medicine. Pp. 113-133. London: Routledge.

Gatchalian, Salvacion with Yafu Yao, Benli Zhou, Lei Zhang, Sutee Yoksan, Kim Kelly, Kathleen M. Neuzil, Mansour Yaïch, and Julie Jacobson.
2008 Comparison of the Immunogenicity and Safety of Measles vaccine Administered Alone or with Live, Attenuated Japanese Encephalitis SA 14-14-2 vaccine in Philippine infants. Vaccine 26 (18): 2234-2241.

Geertz, Clifford
1972 Deep Play: Notes on the Balinese Cockfight. Daedalus 101(1 Winter).

Gehring U with J. Heinrich, G. Hoek, M. Giovannangelo, E. Nordling, T. Bellander T, et al.
2007 Bacteria and Mould Components in House Dust and Children's Allergic Sensitisation. European Respiratory Journal 29:1144-53.

Gehring, U with M. Strikwold, D. Schram-Bijkerk, G. Weinmayr, J. Genuneit, G. Nagel, et al.
2008 Asthma and Allergic Symptoms in Relation to House Dust Endotoxin: Phase Two of the International Study on Asthma and Allergies in Childhood (ISAAC II). Clinical Experimental Allergy 38:1911-20.

Gereda Jose E. with Donald Leung, Andrew H. Liu
2000a Levels of Environmental and Prevalence of Atopic Disease. JAMA 284:1652-3.

Gereda JE, with D.Y. Leung, A. Thatayatikom, J.E. Streib, M.R. Price, M.D. Klinnert, et al.
2000b Relation Between House-Dust Endotoxin Exposure, Type 1 T-cell Development, and Allergen Sensitization in Infants at High Risk of Asthma. Lancet 355:1680-3

Gibbs RA, with J Rogers, MG Katze, R Bumgarner, GM Weinstock, ER Mardis, KA Remington, et al.
2007 Evolutionary and Biomedical Insights from the Rhesus Macaque Genome. Science 316 (5822): 222-34.

Glaser, R
1998 The Influence of Psychological Stress on the Immune Response to Vaccines. Annals-New York Academy of Sciences 840, 649 - 655.

Goldenfeld, Nigel with Aishe Kurti, Keith Whitlock, John Fryer, Patricio Jeraldo, Jeffrey Woods, Nicholas Chia, et al.
2014 Diet and Exercise Orthogonally Alter the Gut Microbiome and Reveal Independent Associations with Anxiety and Cognition. Molecular Neurodegeneration 9 (1): 1-12.

Good, Byron J.
1977 The Heart of What's the Matter: The Semantics of Illness in Iran. Culture, Medicine and Psychiatry: An International Journal of Comparative Cross-Cultural Research. 1 (1): 25-58.

Grandin, Temple and Catherine Johnson
2009 Animals Make us Human: Creating the Best Life for Animals. Boston: Houghton Mifflin Harcourt.

Gravlee, Clarence, C.
2009 How Race Becomes Biology: Embodiment of Social Inequality. American Journal of
Physical Anthropology 139, 1, 47-57.

Green, Judith
2012 One Health, One Medicine, and Critical Public Health. Critical Public Health 22: 377–381.

Guest, Greg, with Arwen Bunce, and Laura Johnson
2006 How Many Interviews Are Enough? An Experiment with Data Saturation and Variability. Field Methods 18 (1).

Hacking, Ian
1999 Madness: Biological or Constructed? *In* The Social Construction of What? Pp. 109-124.
Cambridge, Mass: Harvard University Press.

Hanke, Thomas
2006 Lessons from TGN1412. Lancet 368:1569-70

Hanski, Iikka with Leena von Hertzen, Nanna Fyhrquist, Kaisa Koskinen, Kaisa Torppa, Tiina Laatikainen, Piia Karisola, et al.
2012 Environmental Biodiversity, Human Microbiota, and Allergy are Interrelated. Proceedings of the National Academy of Sciences of the United States of America 109 (21): 8334-9.

Haraway, Donna
2003 A Companion Species Manifesto: Dogs, People, and Significant Otherness. Chicago: Prickly Paradigm.
2004 [1985]. A Manifesto for Cyborgs: Science, Technology, and Socialist Feminism in the 1980s. The Haraway Reader. London: Routledge.
2008 When Species Meet. Minneapolis: University of Minnesota Press.

Hare Brian, Josep Call, Bryan Agnetta and Michael Tomasello
2000 Chimpanzees Know What Conspecifics Do and Do Not See. Animal Behaviour 59:771–786.

Haroon, Ebrahim with Charles L. Raison, and Anderw H. Miller
2012 Psychoneuroimmunology Meets Neuropsychopharmacology: Translational Implications of The Impact of Inflammation on Behavior. Neuropsychopharmacology 37(1):137–62.

Harris, Marvin
1966 The Cultural Ecology of India's Sacred Cattle. In Current Anthropology 7:51-66.

Harrison, Peter
1992 Descartes on Animals. The Philosophical Quarterly 42:167 Pp. 219–227

Hart, Benjamin L. and Karen L. Powell
1990 Antibacterial Properties of Saliva: Role in Maternal Periparturient Grooming and in Licking Wounds. Physiology & Behavior 48 (3): 383-386.

Havstad, Suzanne with Christine Cole Johnson, Haejin Kim, Albert M. Levin, Edward M. Zoratti, Christine L.M. Joseph, Dennis R. Ownby, Ganesa Wegienka
2014 AtopicP Identified with Latent Class Analyses at Age 2 years. Journal of Allergy and Clinical Immunology 134:3, 722

Heijtza, Rochellys D. with Shugui Wang, Farhana Anuar, Yu Qian, Britta Bjorkholm, Annika Samuelsson, et al.
2011 Normal Gut Microbiota Modulates Brain Development and Behavior. Proceedings of the National Academies of Science 108(7):3047–52.

Hertzman, Clyde and Tom Boyce
2010 How experience gets under the skin to create gradients in developmental health.

Annual Review of Public Health 31, 329-47.

Herzog, Harold
2010 Some We Love, Some We hate, Some We Eat: Why It's So Hard to Think Straight About
Animals. New York, NY: Harper.
2011 "The Impact of Pets on Human Health and Psychological Well-Being: Fact, Fiction, or
Hypothesis?" Current Directions in Psychological Science 20 (4): 236-239.

Hinchliffe, Steve, John Allen, Stephanie Lavau, Nick Bingham, and Simon Carter
2012 Biosecurity and the Topologies of Infected Life: From Borderlines to Borderlands. Transactions of the Institute of British Geographers.

Herzog, Harold
2010 Some We Love, Some We Hate, Some We Eat: Why It's So Hard to Think Straight About Animals. Harper Collins: New York, New York.

Heyes, C.M.
1998 Theory of Mind in Nonhuman Primates. Behavioral and Brain Sciences 21: 101-108.

Hodgson, Kate and Marcia Darling
2011 Zooeyia: An Essential Component of "One Health." The Canadian Veterinary Journal 52(2):189-191.

Hoisington, Andrew J., Lisa A. Brenner, Kerry A. Kinney, Teodor T. Postolache, and Christopher A. Lowry
2015 The Microbiome of the Built Environment and Mental Health. Microbiome 3:60

Horai, Reiko with Carlos R. Zárate-Bladés, Patricia Dillenburg-Pilla, Jun Chen, Jennifer L. Kielczewski, Phyllis B. Silver, et al.
2015 Microbiota-Dependent Activation of an Autoreactive T cell Receptor Provokes Autoimmunity in an Immunologically Privileged site. Immunity. 2015;43(2):343–53.

International Conference on Harmonization (ICH)
1998 ICH Efficacy Topic E5. Response Vol. 1998.

Ingold, Tim
1988 The Animal in the Study of Humanity. *In* What Is an Animal? Tim Ingold, ed. Pp. 84–99. London: Routledge.
1990 An Anthropologist Looks at Biology. Man 25(2):208–229.

Inhorn, Marcia and Peter J. Brown
1990 The anthropology of infectious disease. Annual Rev Anthropology 19:89–117

Institute of Medicine (U.S.)
2005 Complementary and Alternative Medicine in the United States. Washington, D.C.: National Academies Press. http://public.eblib.com/choice/publicfullrecord.aspx?p=3377936.

International Primatological Society
2007 International Guidelines for the Acquisition, Care and Breeding of Nonhuman Primates. http://www.internationalprimatologicalsociety.org/docs/ips_international_guidelines_for_the_acquisition_care_and_breeding_of_nonhuman_primates_second_edition_2007.pdf Accessed April 30th, 2016.

Iseki, S.
2001 Future development in Japan. Drug Information Association Meeting. Philadelphia.

Jhee, S., Rosenthal, M. H., Moran, S., & Ereshefsky, L.
2006 *Accelerating Global Drug Development: The Science and Practice of Ethnobridging* (2nd ed.). Glendale, CA: California Clinical Trials.

Joy, Melanie
2010 Why we Love Dogs, Eat Pigs, and Wear Cows: An Introduction into Carnism. San Francisco, CA: Red Wheel/Weiser.

Kahn, Jeffrey
2006 Harmonizing Race : Competing Regulatory Paradigms of Racial Categorization in International Drug Development. Santa Clara Journal of International Law 1, 34-56.

Kant, Immanuel.
1956 (1785) Groundwork of the Metaphysics of Morals. New York: Harper Torchbooks
1993 (1788) Critique of Practical Reason. Upper Saddle River, NJ: Prentice Hall.

Karimi, Karimi with Mark D. Inman, John Bienenstock and Paul Forsythe
2009 Lactobacillus Reuteri Induced Regulatory T cells Protect Against an Allergic Airway Response in Mice. American Journal of Respiratory and Critical Care Medicine 179(3):186–93

Kelly, Kimberly and Mark Nichter
2012 The Politics of Local Biology in Transnational Drug Testing: Creating (Bio)Identities and Reproducing (Bio)Nationalism through Japanese "Ethnobridging" Studies. Asian Science, Technology and Society: An International Journal 6:379–399

Kirksey, S. Eben and Stefan Helmreich

2010 The Emergence of Multispecies Ethnography. Cultural Anthropology. 25 (4): 545-576.

Kirmayer, Lawrence. J.
2002 Psychopharmacology in a Globalizing World: The Use of Antidepressants in Japan. Transcultural Psychiatry 39(3), 295-322.

Koch, Erin
2013 Tuberculosis is a Threshold: The Making of a Social Disease in Post-Soviet Georgia. Medical Anthropology 32 (4): 309-24.

Kontos, Pia C.
1998 Resisting Institutionalization: Constructing Old Age and Negotiating Home. Journal of Aging Studies 12 2: 167-84.
1999 Local Biology: Bodies of Difference in Aging Studies. Aging and Society 19: 677-689.

Kotrschal, Kurt, and Brita Ortbauer
2003 Behavioral Effects of the Presence of a Dog in a Classroom. Anthrozoos: A Multidisciplinary Journal of the Interactions of People & Animals 16 (2): 147-159.

Kirmayer, Laurence J.
2002 Psychopharmacology in a Globalizing World: The Use of Antidepressants in Japan. Transcultural Psychiatry. 39 (3).

Kirsch, Irving
1997 Specifying Nonspecifics. *In* The Placebo Effect: An Interdisciplinary Exploration. Pp.
166-186. Cambridge, MA: Harvard University Press.

Krieger, Nancy and George Davey Smith
2003 Theories for Social Epidemiology in the Twenty-first Century: An Ecosocial Perspective. *In:* Hofrichter, R (ed). Health and Social Justice: Politics, Ideology, and Inequity in the Distribution of Disease – A Public Health Reader. San Francisco: Jossey-Bass, 2003; 428-450.
2004 "Bodies Count" and Body Counts: Social Epidemiology and Embodying Inequality. *Epidemiologic Reviews* 26 (1): 92-103.
2005 Embodiment: A Conceptual Glossary for Epidemiology. Journal of Epidemiology and Community Health 59(5), 350-5.
Krieger, Nancy, Chen, Judy T., Waterman, P. D., Rehkopf, D. H., & Subramanian, S. V.
2005 Painting a Truer Picture of US Socioeconomic and Racial/Ethnic Health Inequalities: The Public Health Disparities Geocoding Project. American Journal of Public Health 95(2), 312-23.

Lacan, Jacques

1968 The Language of the Self: The Function of Language in Psychoanalysis, translated with notes and commentary, by Anthony Wilden. Baltimore, MD: Johns Hopkins University Press.

Lakoff, Andrew
2008 The Right Patients for the Drug: Pharmaceutical Circuits and the Codification of Ilness. In E. J. Hackett, O. Amsterdamska, M. Lynch, & J. Wajcman (Eds.), The handbook of science and technology studies. 3rd ed., Pp. 741-760. Cambridge Mass. MIT Press.

Latour, Bruno
1983 Give Me a Laboratory and I will Raise the World. *In* Science Observed, edited by Karin. D. Knorr-Cetina and Michael. Mulkay, eds. Pp. 141–170. Beverly Hills: Sage.
1991 Technology Is Society Made Durable. *In* John Law ed., Sociology of Monsters. New York: Routledge.
1992 Where are the Missing Masses? The Sociology of a Few Mundane Artefacts. *In* Shaping Technology/Building Society, Wiebe Bijker and John Law, eds. Pp. 228–245. London: MIT Press.
2004 Politics of nature: how to bring the sciences into democracy. Cambridge, Mass: Harvard University Press.
2005 Reassembling the Social: An Introduction to Actor-Network-Theory. Oxford: Oxford UP.

Laland, Kevin, John Odling-Smee, and Sean Myles
2010 How Culture Shaped the Human Genome: Bringing Genetics and the Human Sciences Together. Nature Reviews. Genetics 11 (2): 137-48.

Landis, Story C. with Susan G.Amara, Khusru Asadullah, Chr.is P Austin, Robi Blumenstein, Eileen W. Bradley, Ronald G. Crystal, et al.
2012 A Call for Transparent Reporting to Optimize the Predictive Value of Preclinical Research. Nature 490 (7419): 187-91.

Lauber, Bruce, with Melissa Anthony, and Barbara Knuth
2001 Gender and Ethical Judgments about Suburban Deer Management. Society and Natural Resources 14 (7) 571–83.

Lavenda, Robert H., and Emily A. Schultz
2007 Core Concepts in Cultural Anthropology. Boston, Mass: McGraw-Hill.

Leach, Edmund, R.
1964 Anthropological Aspects of Language: Animal Categories and Verbal Abuse. In New Directions in the Study of Language, ed. E.H. Lenneberg, 23-63. Cabridge, Mass.: MIT Press.

Lee, Yun Kyung with Juscilene S. Menezes, Yoshinori Umesaki, Sarkis K. Mazmanian

2011 Proinflammatory T-cell Responses to Gut Microbiota Promote Experimental Autoimmune
Encephalomyelitis. Proceedings of the National Academy of Science U S A. 108:4615–
22.

Lévi-Strauss, Claude
1963 Structural Anthropology. Translated by Claire Jacobson and Brooke Grundfest Schoepf. New York: Doubleday Anchor Books.
1969 The Elementary Structures of Kinship. Translated by. J.H. Bell, J.R. von Sturmer, and R. Needham. Boston: Beacon Press.

Levy, Stuart B
2002 The Antibiotic Paradox: How the Misuse of Antibiotics Destroys Their Curative Power. Cambridge, MA: Perseus Pub.

Lewis, Jamie, Atkinson, Paul, Harrington, Jean, Fetherstone, Katie
2012 Representation and Practical Accomplishment in the Laboratory: When is an Animal Model *Good-enough*? Sociology 47(4): 776-792.

Lewith, George T. with Wayne B. Jonas and Harald Walach, eds.
2011 Clinical Research in Complementary Therapies: Principles, Problems and Solutions. New
York: Elsevier

Liccardi Gennaro with Gennaro D'Amato, Luciana D'Amato, Antonello Salzillo, Amedeo Piccolo, De Napoli Iolandi, Bruno Dente, and Mario Cazzola
2005 The Effect of Pet Ownership on the Risk of Allergic Sensitisation and Bronchial Asthma. Respiratory Medicine 99 (2): 227-33.

Lock, Margaret
1995 Encounters with Aging: Mythologies of Menopause in Japan and North America. Berkeley: University of California Press.
2013 The Epigenome and Nature/Nurture Reunification: A Challenge for Anthropology. Medical Anthropology 32 (4).

Lock, Margaret and Patricia Kaufert
2001 Menopause, Local Biologies, and Cultures of Aging. American Journal of Human Biology 13: 494-504.

Lock, Margaret and Vinh-Kim Nguyen
2010 Local Biologies and Human Difference. Chapter 4 in: An Anthropology of Biomedicine.
Malden, MA: Wiley-Blackwell. Pp.83-110.

Lupien, S.J., with S. King, MlJ Meaney, and B.S. McEwen.

2001 Can poverty get under your skin? Basal cortisol levels and cognitive function in children from low and high socioeconomic status. Development and Psychopathology 13:653-676.

Low, Gail Ching
1996 White Skins/Black masks: Representation and Colonialism. London: Routledge.

Lynch, Susan V., with Robert A. Wood, Homer Boushey, Leonard B. Bacharier, Gordon R. Bloomberg, Meyer Kattan, George T. O'Connor, et al.
2014 Effects of Early-life Exposure to Allergens and Bacteria on Recurrent Wheeze and Atopy in Urban Children. The Journal of Allergy and Clinical Immunology 134 (3): 593-601.e12.

Lyons, Derek E., and Laurie R. Santos
2006 Ecology, Domain Specificity, and the Origins of Theory of Mind: Is Competition the Catalyst?. Philosophy Compass 1, 481–492.

Mak, Isabella WY with Nathan Evaniew, and Michelle Ghert.
2014 Lost in Translation: Animal Models and Clinical Trials in Cancer Treatment. American Journal of Translational Research 6.2: 114–118.

Marchetti S, and JH Schellens
2007 The Impact of FDA and EMEA Guidelines on Drug Development in Relation to Phase 0 Trials. British Journal of Cancer 97 (5): 577-81.

Martin, Bronwen with Sunggoan Ji, Stuart Maudsley, and Mark P. Mattson
2010 "Control" Laboratory Rodents are Metabolically Morbid: Why it Matters. Proceedings of the National Academy of Sciences of the United States of America. 107 (14): 6127-33.

Martin, Emily
1994 Flexible Bodies: Tracking Immunity in American Culture from the Days of Polio to the Age of AIDS. Boston, Beacon Press.
1997 Designing Flexibility: Science and Work in an Age of Flexible Accumulation. Science as Culture 28: 327-362.
1990 Toward an Anthropology of Immunology: The Body as Nation State. Medical Anthropology Quarterly 4 (4): 410-426.
2013 Enhancing the Public Impact of Ethnography. Social Science and Medicine 99:205-208

Matthews, Robert A J.
2008 Medical Progress Depends on Animal Models - Doesn't It? Journal of the Royal Society of Medicine 101 (2): 95–98.

Mayo Clinic Website
2016 Antibiotics: Misuse Puts You and Others at Risk. http://www.mayoclinic.org/healthy-

lifestyle/consumer-health/in-depth/antibiotics/art-20045720 Accessed May 1, 2016.

McGonigle, Paul
2014 Animal Models of CNS Disorders. Biochemical Pharmacology 87 (1): 140–49.

McDade, Thomas W.
2002 Status Incongruity in Samoan Youth:A Biocultural Analysis of Culture Change, Stress, and Immune Function. *Medical anthropology quarterly*, *16*(2), 123-50.

McDade, Thomas W., Julienne Rutherford J, Linda Adair, and Christopher W. Kuzawa
2010 Early Origins of inflammation: Microbial Exposures in Infancy Predict Lower Levels of
C-reactive Protein in Adulthood. Proceedings of Biological Sciences 277(1684):1129–37.

McEwen, Bruce S.
2003 Early Life influences on Life-long Patterns of Behavior and Health. Mental Retardation and Developmental Disabilities Research Reviews 9:149-154.

McEwen, Scott A.
2006 Antibiotic Use in Animal Agriculture: What Have We Learned and Where are We Going? Animal Biotechnology 17 (2): 239-250.

McFarland Lynne V.
2006 Meta-analysis of Probiotics for the Prevention of Antibiotic Associated Diarrhea and the Treatment of Clostridium Difficile Disease. The American Journal of Gastroenterology 101 (4): 812-22.

McGonigle, Paul and Bruce Ruggeri
2014 Animal Models of Human Disease: Challenges in Enabling Translation. Biochemical Pharmacology 87 (1). Elsevier Inc.

McKenzie R, Fried MW, Sallie R, Conjeevaram H, Di Bisceglie AM, Park Y, et al.
1995 Hepatic Failure and Lactic Acidosis due to Fialuridine (FIAU), an Investigational Nucleoside Analogue for Chronic Hepatitis B. New England Journal Medicine 333:1099-105.

Melby, Melissa K
2005 Vasomotor Symptom Prevalence and Language of Menopause in Japan Menopause 12 (3).

Merleau-Ponty, Maurice
1995 [1956-1960] La Nature. Notes cours du Collège de France. París: Seuil.

Meyer, Urs A.
2002 Introduction to Pharmacogenomics: Promises, Opportunities, and Limitations. In J. Licinio & M.-L. Wong, eds., Pharmacogenomics: The search for Individualized Therapies (pp. 1-7). Weinheim, FRG: Wiley-Blackwell.

Miniello Vito L., with Luigia Brunetti, Riccardina Tesse, Miria Natile, Lucio Armenio and Ruggiero Francavilla
2010 Lactobacillus Reuteri Modulates Cytokines Production in Exhaled Breath Condensate of Children with Atopic Dermatitis. Journal of Pediatric Gastroenterology & Nutrition 50(5):573–6.

Mintz, Sidney W. and Christine M. Du Bois
2002 The Anthropology of Food and Eating. Annual Review of Anthropology 31: 99–119.

Miller, Andrew and Charles L. Raison
2015 Are Anti-inflammatory Therapies Viable Treatments for Psychiatric Disorders? Where the Rubber Meets the Road. JAMA Psychiatry 72(6):527–8.

Miller, Kelly and Tara McGee
2001 Toward Incorporating Human Dimensions Information into Wildlife Management Decision-making' Human Dimensions of Wildlife 6 (3) 205–21.

Millman, Oliver
2016 Anthropomorphis: How Much Humans and Animals Share is Still Contested. The Guardian January 15th, 2016. https://www.theguardian.com/science/2016/jan/15/anthropomorphism-danger-humans-animals-science Accessed April 30th, 2016

Mitchell, Robert and Catherine Waldby
2010 National Biobanks: Clinical Labor, Risk Production, and the Creation of Biovalue. Science, Technology, & Human Values 35 (3): 330-355.

Monnier, Louis, Lapeyronie Hospital, Emilie Mas, Christine Ginet, Lapeyronie Hospital, Laetitia Villon, Lapeyronie Hospital, Jean-paul Cristol, and Claude Colette
2006 Translation of Animal Reserach Into Humans. JAMA 296 (14): 1–4.

Mullin, Molly
1999 Mirrors and Windows: Sociocultural Studies of Human-Animal Relationships. Annual Review of Anthropology 28:201–224.
2002 Animals in Anthropology. Society and Animals 10(4):378–393.

Mullane, Kevin, and Michael Williams
2013 Alzheimer's Therapeutics: Continued Clinical Failures Question the Validity of the Amyloid Hypothesis-but What Lies Beyond? Biochemical Pharmacology 85 (3): 289–305.

Myerhoff, Barbara
1992 Aging and the Aged in Other Cultures: An Anthropological Perspective. *In* Remembered Lives: the Work of Ritual, Storytelling, and Growing Older. Kaminsky, M. ed., Ann Arbor: University of Michigan Press.

Nakajima, M
2001 Relationship Between Interindividual Differences in Nicotine Metabolism and CYP2A6 Genetic Polymorphism in Humans. Clinical Pharmacology and Therapeutics 69(1).

Nash, Roderick
1989 The Rights of Nature: A History of Environmental Ethics. Madison: University of Wisconsin Press.

National Institutes of Health
2011 Statement by NIH Director Dr. Fancis Collins on the Institute of Medicine Report Addressing the Scientific Need for the Use of Chimpanzees in Research. https://www.nih.gov/news-events/news-releases/statement-nih-director-dr-francis-collins-institute-medicine-report-addressing-scientific-need-use-chimpanzees-research Accessed April 30th, 2016.

National Public Radio
2012 Pet Therapy: How Animals and Humans Heal Each Other. March 5th, 2012. http://www.npr.org/sections/health-shots/2012/03/09/146583986/pet-therapy-how-animals-and-humans-heal-each-other Accessed may 1, 2016.
2015 Wherever You Go, Your Personal Cloud of Microbes Follows. September 22, 2015. http://www.npr.org/sections/health-shots/2015/09/22/441841735/wherever-you-go-your-personal-cloud-of-microbes-follows Accessed May 1, 2016.

Nerlich, Brigitte, and Iina Hellsten
2009 Beyond the Human Genome: Microbes, Metaphors and What It Means to Be Human in an Interconnected Post-Genomic World. New Genetics and Society 28, no. 1: 19-36.

Nichter, Mark
2008 Global Health: Why Cultural Perceptions, Social Representations, and Biopolitics Matter.
Tucson: University of Arizona Press.

Nichter, Mark and Jennifer Jo Thompson

2006 For my wellness, not just my illness: North Americans' Use of Dietary Supplements. Culture, Medicine and Psychiatry 30(2): 175-222.

Ohnuki-Tierney, Emiko
1984 Illness and Culture in Contemporary Japan: An Anthropological View. Cabridge, MA: Cambridge University Press.

Olmert, Meg D.
2009 Made for Each other: The Biology of the Human-Animal Bond. Cambridge, MA: Da Capo Press.

One Health Initiative
2016 One Health Initiative Will Unite Human and Veterinary Medicine. http://www.onehealthinitiative.com/ accessed April 29, 2016.

O'Collins, Victoria E, Malcolm R Macleod, Geoffrey A Donnan, Laura L Horky, Bart H van der
Worp and David W Howells
2006 1,026 Experimental Treatments in Acute Stroke. Annals of Neurology 59 (3): 467–77.

O'Sullivan, Orla with Owen Cronin. Siobhan F. Clarke, Eileen F. Murphy, Michael Molloy, Fergus Shanahan, and Paul D. Cotter
2015 Exercise and the Microbiota. Gut Microbes 6(2), 131–136.

Oscarson, M.
1999a Identification and characterisation of novel polymorphisms in the CYP2A locus: implications for nicotine metabolism. FEBS Letters 460(2).
1999b Characterisation and PCR-based detection of a CYP2A6 gene deletion found at a high frequency in a Chinese population. FEBS Letters 448(1).

Park, Alice
2012 Study: Why Dogs and Cats Make Babies Healthier. Time Magazine, July 9th, 2012. http://healthland.time.com/2012/07/09/study-why-dogs-and-cats-make-babies-healthier/ Accessed May 1, 2016.

Perel, Pablo, Ian Roberts, Emily Sena, Philipa Wheble, Catherine Briscoe, Peter Sandercock, Malcolm Macleod, Luciano E Mignini, Pradeep Jayaram, and Khalid S Khan
2007 Comparison of Treatment Effects between Animal Experiments and Clinical Trials: Systematic Review. BMJ Clinical Research Ed 334 (7586): 197.

Petryna, Adriana
2009 When Experiments Travel: Clinical Trials and the Global Search for Human Subjects. Princeton: Princeton University Press.

Pike, Ivy L.
2005. Maternal and Fetal Stress: Evolutionary Perspectives on Preterm Delivery. American Journal of Human Biology 17(1): 45-54.
Pollan, Michael
2013 Some of My Best Friends are Germs. New York Times Magazine, May 15th, 2013. http://www.nytimes.com/2013/05/19/magazine/say-hello-to-the-100-trillion-bacteria-that-make-up-your-microbiome.html?_r=0 Accessed May 1, 2016.

Pound, Pandora, Shah Ebrahim, Peter Sandercock, Michael B Bracken, and Ian Roberts
2004 Where Is the Evidence That Animal Research Benefits Humans? BMJ : British Medical Journal 328 (7438): 514–17.
Povinelli, Daniel J. and Jennifer Vonk
2003 Chimpanzee Minds: Suspiciously Human. Trends in Cognitive Sciences 7:4, 157-160.

Premack, David and Guy Woodruff
1978 Does the Chimpanzee Have a Theory of Mind? The Behavioral and Brain Sciences 4: 515-526

Premack, David
2007 Human and Animal Cognition: Continuity and Discontinuity. Proceedings of the National Academy of Sciences of the USA, 104, 13861–13867.

Prüfer, Kay with Kasper Munch, Ines Hellmann, Keiko Akagi, Jason R. Miller, Brian Walenz, Sergey Koren, et al.
2012 The Bonobo Genome Compared with the Chimpanzee and Human Genomes. Nature. 486 (7404): 527-31.

Raison, Charles L., with Christopher A. Lowry, and Graham A.W. Rook
2010 Inflammation, Sanitation, and Consternation: Loss of Contact with Coevolved, Tolerogenic Microorganisms and the Pathophysiology and Treatment of Major Depression. Archives of General Psychiatry 67(12):1211–24.

Rappaport, Roy A
1968 Pigs for the Ancestors: Ritual in the Ecology of a New Guinea People. New Haven, Connecticut: Yale University Press.

Ravel, Jacques with Pawel Gajer, Zaid Abdo, G. Maria Schneider, et al.
2011 Vaginal Microbiome of Reproductive-age Women. Proceedings of the National Academy of Sciences, USA 108(Suppl 1): 4680–4687.

Regan, Tom and Peter Singer.
1989 Animal rights and human obligations Englewood Cliffs, N.J.: Prentice Hall.

Reardon, Sara

2015 NIH to Retire All Research Chimpanzees. Nature November 18th, 2015. Accessed January 9th, 2016 http://www.nature.com/news/nih-to-retire-all-research-chimpanzees-1.18817

Rock, Melanie, with Bonnie J. Buntain, Jennifer M. Hatfield, and Benedikt Hallgrímsson
2009 Animal-Human Connections, "One Health," and the Syndemic Approach to Prevention. Social Science & Medicine 68 (6): 991-995.

Rock, Melanie with Chris Degeling, and Gwendolyn Blue
2014 Toward Stronger Theory in Critical Public Health: Insights from Debates Surrounding Posthumanism. Critical Public Health 24 (3): 337-348.

Rook, Graham A. W.
2010 Darwinian Medicine and the "Hygiene" or "Old Friends" Hypothesis. Clinical Experimental Immunology 160:70-9.

Rook, Graham A.W. with Charles L. Riason and Christopher A. Lowry.
2013 Childhood Microbial Experience, Immunoregulation, Inflammation and Adult Susceptibility to Psychosocial Stressors and Depression in Rich and Poor Countries. Evolutionary Medicine and Public Health (1):14–7.
2014 Microbiota, Immunoregulatory Old Friends and Psychiatric Disorders I*n:* Microbial Endocrinology: The Microbiota-Gut-Brain Axis in Health and Disease. Lyte, Mark and John F. Cryan, eds. Pp. 319-356.

Rose, Nicholas and Carlos Novas
2005 Biological Citizenship. *In:* Global Assemblages: Technology, Politics, and Ethics as Anthropological Problems. Ong, Aihwa and Stephen J. Collier, eds. Malden, MA: Blackwell Pub.

Ross, Eric Barry, with Margaret L. Arnott, Ellen B. Basso, Stephen Beckerman, Robert L. Carneiro, et. al.
1978 Food Taboos, Diet, and Hunting Strategy: The Adaptation to Animals in Amazon Cultural Ecology. *Current Anthropology* 19.1:1–36.

Rottem, Menachem, Martine Szyper-Kravitz, and Yehuda Shoenfeld
2005 Atopy and Asthma in Migrants. International Archives of Allergy and Immunology 136.2 198-204.

Ruckle, John
2009 Bridging Studies in Pharmaceutical Safety Assessment. Clinical Trials Handbook Pp. 733-768. Hoboken, NJ: John Wiley & Sons.

Sahlins, Marshall
1976 The Use and Abuse of Biology: An Anthropological Critique of Sociobiology. Ann Arbor: University of Michigan Press.

Sands, T. M.
2001 Drug Information Association Meeting. Japan Reimbursement: Rules and Reform in Changing Regulatory Environment. Philadelphia, Pennsylvania

Sanger Institute
2002 The Measure of Man. http://www.sanger.ac.uk/news/view/2002-12-05-the-measure-of-man Accessed April 30th, 2016.

Scheper-Hughes, Nancy
2002 Bodies for Sale – Whole or in Parts. In: Commodifying bodies. Scheper-Hughes, Nancy
and Loïc J. D. Wacquant, eds. Pp. 31-62. London: Sage Publications.

Seed, Amanda and Michael Tomasello
2010 Primate Cognition. Topics in Cognitive Science 2, 407–419.

Sena, Emily S., H. Bart van der Worp, Philip M W Bath, David W. Howells, and Malcolm R. Macleod
2010 Publication Bias in Reports of Animal Stroke Studies Leads to Major Overstatement of Efficacy. PLoS Biology 8 (3).

Seok, Junhee, H Shaw Warren, Alex G Cuenca, Michael N Mindrinos, Henry V Baker, Weihong Xu, Daniel R Richards, et al.
2013 Genomic Responses in Mouse Models Poorly Mimic Human Inflammatory Diseases. Proceedings of the National Academy of Sciences of the United States of America 110 (9): 3507–12.

Shapiro, Kenneth J.
2002 The State of Human-Animal Studies: Solid, At the Margin! Society and Animals 10(4): 331-337.
2001 A Rodent for Your Thoughts: The Social Construction of Animal Models. *In*: Animals in Human Histories. M. Henninger-Voss, ed. Pp. 439-470. Rochester NY: University of Rochester.

Schuelke, S. T., Trask, B.,Wallace, C., Baun, M. M., Bergstrom, N., & McCabe, B.
1991 The Physiological Effects of the Use of a Companion Dog as a Cue to Relation in Diagnosed Hypertensives. The Latham Letter Winter, 14 – 17.

Shell-Duncan, Belinda
1995 Impact of Seasonal Variation in Food Availability and Disease Stress on the Health Status of Nomadic Turkana Children: A Longitudinal Analysis of Morbidity, Immunity, and Nutritional Status. American Journal of Human Biology 7(3), 339-355.

Shir-Vertesh, Dafna

2012 "'Flexible Personhood': Loving Animals as Family Members in Israel." American Anthropologist. 114:(3).

Simpson, Angela and Adnan Custovic
2005 Pets and the Development of Allergic Sensitization. Current Allergy and Asthma Reports. 5 (3): 212-220.

Smith, Carli J. with Jacob R. Emge, Katrina Berzins, Lydia Lung, Rebecca Khamishon, Paarth Shah, et al.
2014 Probiotics Normalize the Gut-Brain-Microbiota Axis in Immunodeficient Mice. American
Journal of Physiology Gastrointestinal and Liver Physioliology 307(8):G793–802.

Smith, Peter A.
2015 The Slobber Cure. Wired Magazine, November 2015.

Song, Se Jin with Christian Lauber C, Elizabeth K. Costello et al.
2013 Cohabiting Family Members Share Microbiota with One Another and With Their Dogs. Weigel D, ed. *eLife*. 2:e00458.

Sorabji, Richard
1993 Animal Minds and Human Morals. New York: University of Cornell Press.

Speaking of Research
2016 The Animal Model: Biological Similarity of Humans and Other Animals. https://speakingofresearch.com/facts/the-animal-model/ Accessed April 30th, 2016.

Statistics Bureau, M. of I. A. and C. J.
2010 Chapter 2 Population. Statistical Handbook of Japan 2010. Retrieved March 18, 2011, from http://www.stat.go.jp/english/data/chouki/02.htm, Accessed March 18th, 2011.

Stiegler, Denise with John D. Gilbert, Morgyn S. Warner, and Roger W. Byard
2010 Fatal Dog Bite in the Absence of Significant Trauma. The American Journal of Forensic Medicine and Pathology. April, 1st.

Steiner, Gary
2005 Anthropocentrism and Its Discontents: The Moral Status of Animals in the History of Western Philosophy. Pittsburgh: University of Pittsburgh Press.

Strachan DP

1989 Hay Fever, Hygiene, and Household Size. BMJ Clinical Research Ed 299 (6710): 1259-60.

Sunder Rajan, Kaushik
2006 Biocapital: The Constitution of Postgenomic Life. Durham, NC: Duke University Press.

Suntharalingam, Ganesh with Meghan R. Perry, Stephen Ward, Stephen J. Brett, Nicki Panoskaltsis, and Michael D. Brunner
2006 Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412. The New England Journal of Medicine. 355 (10).

Tanggaard, Lene
2009 The Research Interview as a Dialogical Context for the Production of Social Life and Personal Narratives. Qualitative Inquiry 15:1498–1515.

Transparency Market Research
2015 Probiotic Market By Application (Food and Beverages ,Dietary Supplements, Animal Feed) By End Users (Human Probiotics, Animal Probiotics)-Global Industry Analysis, Size, Share, Growth and Forecast 2014 - 2020 http://www.transparencymarketresearch.com/probiotics-market.html Accessed may 1st, 2016

Triendl, Robert, and Herbert Gottweis
2008 Governance by Stealth: Large-Scale Pharmacogenomics and Biobanking in Japan. *In* Biobanks: Governance in Comparative Perspective. Herbert Gottweis and Alan Peterssen, eds. Pp. 123–40. New York: Routledge.

Thompson, Jennifer, J. with Cheryl Ritenbaugh and Mark Nichter.
2009 Reconsidering the Placebo Response from a Broad Anthropological Perspective. Culture, Medicine, and Psychiatry 33(1):112-52.

Udani, P. M.
1994 BCG Vaccination in India and Tuberculosis in Children: Newer Facets. Indian Journal of Pediatrics, 61 451-462.

Valeri, Valerio
2000 The Forest of Taboos: Morality, Hunting, and Identity Among the Huaulu of the Moluccas. Madison: University of Wisconsin Press.

Valasquez-Manoff, Moises
2015 Among the Trillions of Microbes in the Gut, a Few are Special. Scientific American March 1, 2015. http://www.scientificamerican.com/article/among-trillions-of-microbes-in-the-gut-a-few-are-special/ Accessed May 2, 2016.

Van Boeckel, Thomas P. with Gandra Sumanth Gandra, Ashok Ashvin, Quentin Caudron, Bryan T Grenfell, Simon A Levin, and Ramanan Laxminarayan
2014 Global Antibiotic Consumption 2000 to 2010: An Analysis of National Pharmaceutical Sales Data. The Lancet Infectious Diseases 14 (8): 742-750.

Van de Weide, J., & Steijns, L.
1999 Cytochrome P450 enzyme system: genetic polymorphisms and impact on clinical pharmacology. Annals of Clinical Biochemistry, 36, 722-9.

van der Vaart, Elske, Hemelrijk, Charlotte
2014 "Theory of Mind" in Animals: Ways to Make Progress. Synthese 191:335-354.

Virga, Vint
2013 The Soul of All Creatures: What Animals Can Teach us About Being Human New York: Crown.

Wagner, Wolfgang
2007 Vernacular Science Knowledge: Its Role in Everyday Life Communication. Public Understanding of Science 16(1): 7-22.

Wahlberg, Ayo
2009 Bodies and Populations: Life Optimization in Vietnam. New Genetics and Society 28 (3): 241–51.

Waldby, Cathy and Robert Mitchell
2006 Tissue Economies: Blood, Organs, and Cell Lines in Late Capitalism. Durham N.C.: Duke University Press.
2010 National Biobanks: Clinical Labor, Risk Production, and the Creation of Biovalue. Science, Technology & Human Values 35(3), 330-355.

Warinner, Christina and Cecil M. Lewis, Jr.
2015 Microbiome and Health in Past and Present Human Populations. American Anthorpologist 117:4, Pp. 740-741.

Wells, Deborah L.
2009 The Effects of Animals on Human Health and Well-Being. Journal of Social Issues 65 (3): 523-543.

West Coast Clinical Trials.
2011 Recruitment Advertisement. http://jp.wcct.com/ Accessed April 1, 2011.

Wilson, Cindy C., and Dennis C. Turner
1998 Companion Animals in Human Health. Thousand Oaks: Sage Publications.

Wolch, Jennifer with Alec Brownlow, and Unna Lassiter
2000 Constructing the Animal Worlds of Inner-City Los Angeles. *In:* Animal Spaces, Beastly Places: New Geographies of Human–Animal Relations. Pp. 71-97. Chris Philo and Chris Wilbert, eds. London and New York: Routledge.

Wolch, Jennifer and Jin Zhang
2005 Siren Songs: Gendered Discourses of Concern for Sea Creatures. *In:* A Companion to Feminist Geography. Lisa Nelson and Joni Seager, eds. Pp. 458–85.Oxford: Blackwell Publishing.

Woolgar, Steve and *Bruno Latour*
1979 Laboratory Life: The Construction of Scientific Facts. Princeton, New Jersey: Princeton University Press. Los Angeles: Sage Publications

Wood, A. J. J., & Zhou, H. H.
1991 Ethnic Differences in Drug disposition and Responsiveness. Clinical Pharmacokinetics 20(5).

World Health Organization.
2016 Zoonoses and the Human-Animal-Ecosystems Interface. http://www.who.int/zoonoses/en/ Accessed on April 29, 2016.

Worthman, Carol M. and Brandon Kohrt.
2005 Receding Horizons of Health: Biocultural Approaches to Public Health Paradoxes. Social science & medicine (1982) 61(4), 861-78.

Wynne, Brian
1992 Misunderstood Misunderstanding: Social Identities and Public Uptake of Science. Public Understanding of Science 1(3): 281-304.

Yandell, Kate
2013 Great Ape Research Decision. The Scientist, March 12, 2013. http://www.the-scientist.com/?articles.view/articleNo/34680/title/Great-Ape-Research-Decision/ Accessed on April 30th, 2016.

Yazdanbakhsh Maria with Peter G. Kremsner and Ronald van Ree
2002 Allergy, Parasites, and the Hygiene Hypothesis. Science 296 (5567): 490-4.