Designing for the Sexes: Accounting for Differences Between Males and Females in Hip Replacement Technology Research and Development and Patient Outcomes

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Introduction

As healthcare faces unprecedented challenges to improve quality, reduce harm, and improve access, the innovation of medical technology is becoming a major focus across the world. With a crucial role in the prevention, treatment, and rehabilitation of illness and disease, medical device technology has accelerated its growth, in part of rapidly expanding scientific research and development (R&D) in the field of medical devices (Gelijns & Medicine, 1989). Despite the growth of R&D, more than 1.7 million injuries and nearly 83,000 deaths across the United States were linked to the failure of medical devices ("Medical Devices Harm Patients Worldwide As Governments Fail On Safety," n.d.). Specifically, females were disproportionately harmed as a result of medical device failures (*Are women more likely to be harmed by medical device failures? - ICIJ*, n.d.).

This paper will focus on hip replacements, one of the best examples of how bias in the R&D process contributes to a higher failure rate for females than for males and highlights a number of factors that may be generalizable. I believe that examining hip replacement through the lens of Social Construction of Technology (SCOT) will provide insights regarding the bias that exists in the R&D process and its influence on the design of medical devices and patient outcomes, from which we might find ways to advance medical treatment, prevention, and diagnosis.

Background & Social Construction of Technology (SCOT)

Currently, medical R&D is growing faster than ever with an increased emphasis on early- stage processes as they are believed to contribute to favorable impacts on patient outcomes (*Research, Develop, Produce, Repeat*, n.d.). The R&D process is directly influenced by human action, specifically stakeholders' decisions such as spending, collaborating, and

adapting to industry and customer needs. The R&D of a medical device is the most crucial phase for determining its success or failure. If a loosely-defined and designed medical device makes it to market, it will fail to deliver its defined functionality and benefits (*Medical Device Design and Development*, 2017).

One specific medical procedure, the hip replacement or total hip arthroplasty, is a surgical procedure to replace a worn-out or damaged hip joint. This surgical approach includes removal of diseased cartilage and bone parts and replacement by the corresponding artificial joint prosthesis or medical device. This procedure is typically chosen to reconstruct hip fractures, correct several forms of osteoarthritis, and invalidate effects of rheumatoid arthritis, birth defects, and post-traumatic states (*Hip Replacement Surgery | Johns Hopkins Medicine*, n.d.).

To analyze the R&D of hip replacements, the SCOT framework will be used. SCOT, a constructivist theory of technology innovation, argues that technology does not determine human action, but rather, human action shapes technology (*Social construction of technology (SCOT)—Stswiki*, 2018). SCOT describes technology innovation as a complex process of co-construction in which technology and society, to the degree that they could even be conceived separately of one another, negotiate the meaning of new technological artifacts, alter technology through resistance, and construct social and technological frames-of-thought, practice and action (Klein & Kleinman, 2002). It is not only a theory, but a methodology that formalizes the steps and principles to follow when one wants to analyze the causes of technological failures or successes. According to SCOT, those who seek to understand the reasons for acceptance or rejection of a technology should look to the social world to see why a certain technology wins out. For any case, including hip replacement research and design, researchers must look at the

criteria for success and the stakeholders who define it. The SCOT framework encapsulates the sociotechnical processes that drive technological change by considering system stakeholders and influences as interacting entities (Klein & Kleinman, 2002).

I will analyze the technology of hip replacements using the SCOT framework and highlight a number of factors that might be generalizable. I will first explain the current approach to R&D of the artificial hip prosthesis. Then, I will look at examples of bias at each stage of R&D and how sex-based bias, or the preference or prejudice towards one sex over the other, impacts device design and patient outcomes (*What is Gender Bias?*, n.d.). The current approach to R&D of the hip prothesis is broken down into three phases. The first phase of the R&D process consists of design and material testing. This includes identification of the needs, model design, FEM assessment, mechanical properties, and biocompatibility testing. The second phase includes fabrication and preparation. Casting and machining, packaging and preparation, preclinical and clinical trials, and regulative work are included in this phase. The final stage of the R&D process includes clinical and pre-clinical use. Specifically, this includes implantation and follow-up as well as post-revision explant analysis (Colic & Sedmak, 2016).

Literature Review

While several scholars have examined bias in the field of medicine, they have not adequately considered the role of sex-based bias on the outcome of medical devices. Many scholars discuss factors such as clinical practice, medical research, education, and 'gender order' in society and their implications in the treatment of patients.

One example that focuses on sex-based bias is a study conducted by Sanket S. Dhruva that studies the Food and Drug Administration (FDA) premarket approval of cardiovascular devices (Dhruva Sanket S. et al., 2011). The study explored the type and quality of sex-specific

data reviewed by the FDA prior to approval by performing a systematic review of the demographics, commenting on sex-based bias, and analyzing of the results by sex for 78 high-risk cardiovascular devices that received FDA approval between 2000 and 2007. Results found that FDA summaries of evidence did not report the sex of enrollees in 28% of the studies. Additionally, the study found that out of the study populations that reported sex distribution, 67% were men (Dhruva Sanket S. et al., 2011). Ultimately, the study found that there is a lack of sex-specific safety and effectiveness data for high-risk cardiovascular devices prior to FDA approval. Overall, they concluded by saying that more rigorous FDA requirements for sex-specific data prior to device approval could present an opportunity to improve cardiovascular outcomes. This study successfully examined the final stage of the R&D process of clinical and preclinical data. However, this study's authors fail to examine the existence of sex-based bias in other phases of the R&D process that contribute to the success or failure of the medical device. Examining the entire workflow or process of R&D could be an important part of understanding differing outcomes of medical technology.

Another study examining sex-based bias in research found that evidence-based medicine may be fundamentally flawed due to an ongoing failure of research tools to include sex differences in design and analysis. This study found a continuation of deep-seated patterns of disadvantage by reviewing several cases of equalities reviews in the UK (Holdcroft, 2007). The study found that reporting bias creates a situation where guidelines based on the study of one sex may be generalizable and applied to both. One specific case that this study examines is the UK Cabinet Office's equality review in November 2005 that discovered that research funding for coronary artery disease in males is far greater than for females. The author explained that the lack of funding for female disease in effect maintains females' lower

economic status and hinders research into sex-based medicine. Additionally, the author examines the sex-based bias in clinical research, clinical trials, and the reporting of sex-specific data. The article focused only on the deep-rooted sex-based bias existing in evidence-based medicine. The article concluded by encouraging the UK to seize the opportunity to implement best practices for health care research across sexes and to establish sex specific evidence-based guidance. This study failed to mention the potential of sex-based bias in other phases of development besides research. Furthermore, the article fails to connect sex-based bias in research to the outcome of the developed product.

Both of these teams of researchers believe that there is existing bias in the field of medicine and encourages the implementation of additional regulations and safe practices in research to attempt to eliminate biases. However, to target only research, is to ignore the influence of sex-based bias in other phases of the development process, ultimately ignoring the factors that contribute to the overall outcome of any medical device. While the currently considered factors of data collection and analysis in research are important to understanding the outcome of a medical device, I will focus my analysis on the influence of sex-based bias on the process of R&D of the hip replacement. I will demonstrate the importance of understanding human actions, specifically sex-based bias, on the overall outcome of medical devices.

Analysis of Hip Replacement Technology R&D and Patient Outcomes

For more than 300,000 people in the United States each year, total hip replacement serves as a surgical approach for the treatment of severe forms of osteoarthritis, birth defects, and post-traumatic stress. However, most implants only last for 10-15 years, and one of the most common problems for both patients and doctors is implant failure (*Hip replacement*

surgery | Treatment options | Versus Arthritis, n.d.). Implant failure may lead to negative attitudes towards medical procedures, technology, and overall healthcare.

The aim of the hip implant design is to mimic the natural human hip. The hip joint is one of the most important load-bearing, shock-resistant structures of the body, particularly during walking, running, and jumping. The design process for the hip replacement must examine the stress-strain transmission as well as short-term and long-term behavior of hip prosthesis. The modern approach to R&D of the artificial hip prosthesis includes three phases: the design, fabrication, and clinical use (Colic & Sedmak, 2016). All three phases in the modern approach of the hip replacement rely on human actions such as decision making and interactions, however, with any human action or any human-dependent system, bias exists.

To account for differences between males and females in hip replacement technology R&D and patient outcomes, SCOT is used to establish human or stakeholder action during the R&D process. R&D, the process of technology design, is an open process that can produce different outcomes for relevant social groups. Relevant social groups or stakeholders include designers of medical devices, physicians, government regulators, and patients. Members of each social group share the same attitude attached to a specific artifact. For the case of the hip replacement, designers develop the technology, physicians install the technology and care about patient healing, and the patients receive the technology to solve a medical problem. The use of a case highlights various considerations important for future policies and demonstrates human factors involved in the R&D of medical devices as well as patient outcomes. Additionally, the following sections demonstrate how sex-based bias exists in each step of the hip replacement's R&D process and how device failure may lead to distrust and negative attitudes towards medical technology.

Design and Material Testing

Design and material testing, the first phase of the current R&D approach for the hip implant, consists of five steps. The first step is the identification of the need for the patient. When developing a novel medical device, particularly one that is patient-centered, it is critical to identify specific patient needs such as materials, functions, and costs. Research has shown that sex-specific differences play a role in the determinants and consequences of health and illness (Vlassoff, 2007). Sex interacts with the social, economic, and biological determinants and consequences of disease and injury to create different health outcomes for males and females. Furthermore, the interaction between biological and social determinants is present when considering sex-specific differences in health. Biological differences may be suppressed by socialization and how society responds to sex-specific behavior. Social norms endorsing behavior can reinforce negative tendencies. These social norms exist due to human action. In the case the hip replacement, there exists significant biological differences based on sex, specifically relating to pelvis geometry (Wang et al., 2004). Pelvis geometry includes socket depth and femoral head width, and each side of the pelvis has a hip joint. In comparison, females have greater socket depth and smaller femoral heads, which ultimately leads to different loading capabilities between male and female hips. Despite this, there is no systematic body of knowledge or design system that identifies specific implant device design needs based on sex. Rather, unique female biological geometries are ignored and male geometries are used for development, despite the fact that more females receive about 56% of hip replacements (*Gender Differences in Total Hip Arthroplasty | Physician's Weekly*, n.d.). This historic tendency represents a bias favoring male geometry when determining patient needs in the first step of R&D. This bias potentially is a large contributor to the differences in successful

outcomes between males and females who have hip replacement surgery.

During the second step, the model design, the designer must consider functions, structures, and needs identified in step one while proceeding to design a model. Structural and functional factors that the designer must take into account differs in males and females. Factors that enhance desirability of a device include increased functionality, increased abilities, and the availability of someone to serve the prosthesis. Oppositely, factors that detract from the desirability of a medical device are appearance, lifestyle incompatibility, weight, need for service, and difficulty to use. Typically, human factors dictate design, playing a crucial role in the final technological product. Currently, the device design of the hip implant is not gendered in appearance nor is it designed with female anatomy in mind. Despite the desired and undesired factors of a patient towards a medical device, the hip replacement designers fail to consider the anatomical needs of females, confirming the sex-based bias existent in its model design due to stakeholder actions.

The next step is characterized by a finite element method (FEM) assessment to obtain a preliminary overview of the expected mechanical proprieties of candidate designs (Colic & Sedmak, 2016). FEM's advantage as a computational method is used to determine the stresses and strain in any given point within a structure with arbitrary geometry and material complexity. Engineers developed the FEM assessment as follows. First, to develop a FEM model, the shape of the implant or bone being analyzed is divided into small elements. For three-dimensional analysis, elementary volumes with certain geometry are used and for two-dimensional analysis, elementary surfaces with specific geometry. Every element has nodes, usually located at the tips of the element and in each node point, three (two for 2D) displacement components are determined along with three (two for 2D) force components.

This model provides a numerical tool for analysis of structures subjected to different types of load. For the case of a hip implant, there are factors that influence the hip implant's integrity and life. Advantages of using FEM in hip implant integrity analysis include its ability to handle complex geometries, types of analysis, and loads, models made of non-homogenous materials, contact surface models, and structural integrity analysis. Despite these advantages, there are factors that influence implant integrity and life that is not possible to include by using FEM. FEM lacks exact mechanical properties of bone, effects of the environment such as organisms, possible complication after hip implantation, allergies, and activity level. In addition, FEM does not consider age and sex-specific differences for the hip implant, two major factors that affect implant integrity and life. FEM's inability to account for age and sex-specific differences may be explained by its design to only consider numerical values to explore stress, strains, and loads. Without the consideration of age and sex, there is no way for the FEM system to capture existing biases as the system itself will only capture mechanical properties. Currently, it is common for numerous model designs to be subjected to FEM assessment to determine which design produces the most favorable expected mechanical properties. From this, the most favorable design would continue to mechanical testing in the next step of the R&D process. In the initial FEM testing phase, all designs are based on male geometries, thus eliminating sex considerations during FEM. Ultimately, human action in the design of FEM model highlights the system's weakness to account for sex-specific differences in analysis.

Mechanical properties testing, the fourth step of R&D's design and material testing, is useful to ensure that the mechanical properties of the implant biomaterials resemble that of real bone and tissues. Mechanical properties testing compares the elastic modulus, yield strength,

and tensile strength of tissues and biomaterials under various conditions. Careful evaluation of the biomaterial properties must be carried out to ascertain whether new designs can guarantee mechanical resistance to physiological load. Mechanical properties influence hip prosthetic's integrity and life. The forces acting on the prosthesis caused by human activity are the result of dynamic stress that varies in time and leads to mechanical fatigue of the implant. A motion capture study was conducted to examine relative risk of impingement and joint instability during physical and sexual activities after a hip replacement. The study discovered that active positions put females at a greater risk of implant failures than males. This was due to the anatomical differences between males and females. Specifically, the male pelvis is generally taller and narrower than the female pelvis. In active positions, females require intensive flexion *(>95°)* which causes prosthetic impingement (Charbonnier et al., 2014). Prosthetic impingement occurs because the prosthetic only accounts for the amount of flexion necessary for a male, thus failing to account for the additional flexion of a female. The case of the hip replacement demonstrates how human action such as physical or sexual activity impacts mechanical properties such as stress and strain. In many cases, increasing stress and strain leads to the failure of a device. In conclusion, current hip implant designs failure to account for the differing mechanical properties between males and females demonstrate a failure of sex-based equality in R&D due to designers' biases.

The final step of the design and material testing of R&D is biocompatibility testing. Biocompatibility testing is performed to ensure that the implant and its materials will be accepted by the human body. When testing for biocompatibility, several characteristics such as the permission of cell encapsulation, viability, and limited toxicity are desired. Sex-specific differences exist in the deposition and toxicity of metals. Health effects of toxic metals differ in

prevalence and manifest differently in males and females. According to research examining bone following arthroplasty of the hip joint, lead and cadmium concentrations were the highest in the cortical bone and cancellous bone, respectively (Lanocha et al., 2012). Specifically, cadmium retention is higher in females than in males and may have estrogenic effects and affect female offspring. Males generally have higher blood lead levels than females. Lead accumulates in bone whereas increased endogenous lead exposure is often found in females who are pregnant or going through menopause. Recent experimental data suggests that females more susceptible to immunotoxin effects of lead than males (Vahter et al., 2007). Consequences of lead buildup include headaches, infertility, seizures, and in extreme cases comas. Applied to the case of the hip replacement, there exists tests for biocompatibility of an implant. *In vitro* assessments are tests performed outside of a living organism, and are appealing due to the low cost, short time duration, and high reproducibility and reliability. Since *in vitro* tests only expose single cell types, their results cannot be directly generalizable to a complex biological system. Therefore, a long term clinical performance, along with studying the tissue reaction to an implant must be conducted. *In vitro* tests fail to take into account sex-specific differences as the experimental focus is only on one cell type's reaction with the implant material. Similarly, long term clinical performance assessments are currently designed to focus on the reaction of the implant material in a single type of organism such as one animal type, rather than exploring how reactions may differ in sex. In both cases of assessment, biocompatibility or the interaction between a medical device and cells or tissues is being tested. However, without recognition to test multiple sexes in subgroups during biocompatibility testing, only one sex is tested. Thus, stakeholders' design of biocompatibility testing of hip implants has no recognition of sex-specific differences. Without recognition of sex-specific differences, any existing biases in the

implant will pass through the first phase of R&D undetected, confirming that technology is shaped by human action or lack-there-of.

Fabrication and Preparation

The second phase of R&D, fabrication and preparation, is made up of four steps: casting and machining, packaging and preparation, preclinical and clinical trials, and regulative work. Specifically, sex-based bias exists during packaging and preparation. Gender by design approaches have been adopted in efforts to increase performativity and appeal packaging to the consumers. The representation of gender on mass-produced packaging represents human actions and biases. For example, on some medical packaging, biological difference between females and males are presented as scientific facts. Non-medical, common products that follow the same gender-targeting packaging method includes Bounce fabric softener sheets "for men", Degree deodorant "for men", and Bic pens "for her". On the other hand, for products such as perfume or makeup packaging, gender is represented as decoupled from the body and part of an enjoyable choice of identity. For the hip implant, packaging and preparation is targeted towards the stakeholders such as hospital representatives and surgeons who purchase and use the device. The patient will not see the packaging of the implant, yet the human action of purchasing one implant over another determines which implant is used and accepted by the surgeon, and therefore impacts the patient's outcome.

The next step of fabrication and preparation is preclinical and clinical trials. When examining historical literature regarding females' involvement in clinical trials, the importance of the consideration between male and female decision-making is clarified. It is evident that in recent decades females are not always adequately enrolled nor is data examined for sex-specific differences. According to a study that evaluated the inclusion of sex in the results of federally-

funded randomized clinical trials in nine major medical journals in 2009, researchers found an average enrollment of 37% females and sex-specific analysis was present in only 13% of studies (Liu & Mager, 2016). In addition, there may be differences in patient outcomes or responses to treatment between males and females (Liu & Mager, 2016). Even if women are represented in clinical trials, many studies do not provide sex-specific analysis because either the study was not powered sufficiently to allow for subgroup analysis or sex-specific analysis was not a part of the hypothesis being tested. This lack of sex representation and subgroup analysis has led to serious consequences. For example, in 2005, 80% of drugs withdrawn from the US market were due to side effects impacting women that had not been studied during initial drug trials (Liu & Mager, 2016). Similar to clinical trials of other medical devices, hip implant clinical trials exhibit sex inequality. Existing hip implant clinical research studies do not provide sex-specific analysis, possibly due to the reasons previously stated; however, it is known that women are underrepresented in clinical studies (Hettrich et al., 2015). Ultimately, the decision of engineers and physicians to focus primarily on males in clinical trials contributes to the differing outcome of the procedure.

The final step focuses on the regulative work involved in R&D. This includes government laws and industrial regulations designed to support the safety and regulation of medical devices. In the United States, the FDA is responsible for protecting public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices (Commissioner, 2018). There are three basic pathways to obtain FDA market approval for medical devices, depending on the nature of the device. The first pathway is the pre-market approval, where device manufacturers are required by law to notify the FDA of their intent to market a medical device. The second pathway, the premarketing notification,

or the 510(k) application is a fast-track process for devices in which the sponsor shows that the device is equivalent to an existing device that is already marketed and approved. The third pathway, the humanitarian device exemption, is one that is expected to treat or diagnose conditions that affect fewer than 4,000 individuals in the United States annually (Van Norman, 2016). The most commonly used pathway, particular for hip implants, the 510(k) process, presents underlying problems. The problem with the 510(k) process is that it allows high-risk devices to be implemented in people without first undergoing human clinical trials. The FDA has utilized the 510(k) process to approve dangerous devices based on predicates, even if that predicate had previously been removed from the market because it had failed (Palumbo, 2018). The FDA did this with metal-on-metal hip replacements which have a high failure rate and produce harmful debris. In terms of demographic-specific information supporting the FDA's approval of high-risk medical devices, only 17% of approved devices included information by sex (Dhruva et al., 2017). Additionally, this means that any new company looking to use a 510(k) will base their product on a previous product that lacks sufficient data on sex-specific differences, thus, furthering existing bias. Ultimately, this highlights the lack of sex-specific information and regulations in the government's regulatory process that continue to shape emerging technologies.

Clinical and Post-Clinical Use

The final phase of R&D, clinical and post-clinical use, is critical for the improvement of diagnoses and treatment of disease or injury. Historically, females have been under-represented in or excluded from clinical studies. This has led to a lack of available data for females and showcases clinical studies' barriers for female enrollment. Barriers include the lack of understanding about main obstacles, fear of fetal consequences if the female becomes pregnant,

and the lack of understanding about differences in disease etiology (Health, 2020).

Two steps make-up the clinical and post-clinical use stage of R&D. These steps are the implantation and follow-up and the post-revision explant analysis. During the first step, the sex of the doctor can make a difference of what the female patient learns about her implant. Low number of female surgeons means patients often see male surgeons ("Hidden curriculum" keeping best and brightest from becoming surgeons, n.d.). Differing sex dyads often play a role in the doctor-patient communication, specifically during the follow-up step. Specifically, female dyads were the most patient-centered and had longer consultations containing the most talk. These sex-based biases can be applied to the case of the hip implant where the patient-doctor relationship contributes to the outcome of the device and the attitude towards medical technology. Measuring outcomes can be divided into three main domains: objective, behavioral, and subjective. Behavioral outcomes include functional status, recovery, and adherence to treatment whereas subjective outcomes include pain, understanding, and satisfaction. The quality of doctor-patient communication impacts outcomes such as the frequency of visits, emotional health, and symptom resolution. The manner in which a physician communicates with a patient influences how a patient responds such as whether patients obey rules. It is critical that the physician gains the patient's trust to support a positive doctor-patient relationship. For the hip replacement, after surgery, patients are ordered by physicians to restrict movements and activities that could damage their implant. Without trust, patients may disobey the physician's order, leading to device failure and patient injury. Without proper communication, a patient may not fully understand medical directions, which in the case of a hip replacement, could lead to harmful movements, and a failed outcome. Therefore, it is evident in that stakeholder actions, such as doctor and patient communication, directly impact the outcome of medical technology.

Human actions and decisions play a major role in all three phases of R&D and patient outcomes. Among 340,000 people whom the FDA listed as being injured by a medical device in 2018, females made up 67%, compared to males at 33% (Report, 2019). In the case of hip implants, the same model is available for males and females, implying these devices are sex neutral; however, females and males have anatomical differences and hip implants are more than twice as likely to fail in females (Hutchison, n.d.).

Ultimately, stakeholder actions play a role in any medical device failure, and the act of failure has devastating results. Stakeholders with different perspectives of the medical system have different criteria for developing trust in medical technologies (Montague et al., 2010). Nonetheless, the failure of the hip replacement may lead to distrust or negative attitude towards medical devices and treatment.

Conclusion

I have argued that sex-based bias influences medical device design and patient outcomes. Specifically, I identified the case of the hip replacement and highlighted a number of generalizable factors. I also identified the phases of R&D and highlighted the existence of bias at each phase. The sex-based bias in the R&D process of medical devices has led to different patient outcomes with females facing greater failure rates, increased injuries, and a greater mistrust in the healthcare system. Whether it is to design a technology, be treated for an injury, or regulate technologies, each stakeholder has his or her own agenda to fulfill paired with biases. From these commonalities, social groups form and often compete with their technological ideas. In the case of the hip replacement, the social group consisting of female patients has not been properly identified, nor have their needs been researched properly. The analysis demonstrated the fundamental flaw to assume that two populations are the same and

the importance of involving representatives from all stakeholder groups including doctors, patients, governments, and engineers during stabilization, the process where multiple groups achieve closure.

The analysis of the hip replacement through the lens of SCOT highlighted that technology is shaped by human action, particularly stakeholder biases, and contribute to technology's success or failure. This analysis is important because, as engineers, doctors, and patients diversify in race, ethnicity, sexual orientation, and gender identity, more bias may be uncovered, either by the introduction of a medical device to empower patients or through the identification of a previously underreported clinical treatment problem. As engineers, it is critical to understand that bias exists with humanity, yet human action can recognize bias and create systematic change in order to produce standards that result in enhanced patient outcomes.

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