

The Co-Participants Model for Fetal Involvement in Research

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Research during pregnancy currently lags behind other types of research. Lucy Langston (2016) attributes a large portion of this issue to hesitancy by Research Ethics Boards (REBs) to approve research involving pregnant people because it is not always clear how the risks and benefits can be balanced between the parent and fetus when their interests may come in conflict. Authors such as Wild and Biller-Andorno (2016) have emphasized that one major reason that it is difficult to balance these risks and benefits is that the status of the fetus in research is unknown. By answering the question of the status of the fetus in various research contexts, we can reduce the hesitancy of researchers and REBs to pursue and approve research during pregnancy and fill in the gaps in medical knowledge in a safe, ethical manner.

I argue that, based on conceptual understandings of terms like “subject” and “participant,” fetuses can fit the role of a research subject when their data is being analyzed for research outcomes, and can therefore be considered participants under the prominent Canadian guidelines known as Tri-Council Policy Statement for Research Involving Humans (TCPS2). Since fetuses are sometimes participants, we should acknowledge them as such when appropriate and take their interests into consideration, while also ensuring that pregnancy alone is not considered a reason to focus on fetal interests. This means protecting fetal interests through proxy consent when the consent process can increase clarity about which role the parent and fetus each play in research, improving respect for the pregnant parent, and welfare for the parent and fetus.

I develop the co-participants model for viewing both the pregnant parent and fetus as individual participants who are inextricably linked. This allows researchers to have obligations to the fetus in the same way they would a born child, but to still take these obligations in conjunction with the pregnant parents’ interests and consider how these needs overlap. The co-participants model is preferable to the “fetus as a patient” model by McCullough and Chervenak (1994, p. 96), and the “double unit” model by Wild (2012, p. 91) because those models use a medical practice definition of patient, and rely on a capacity view of personhood to define participation respectively. Neither model can capture a general descriptive account of what it means to be a participant of research, blurring what that would mean for the fetus.

One major objection to the change in fetal status is the perception that it elevates the moral status of the fetus and could affect vital healthcare involving pregnancy termination. The benefit of my co-

participants model is that it does not rely on any argument of moral personhood to determine which beings count as participants under the TCPS2. The obligations of the researcher to the fetus begin after the pregnant parent has committed their body to the growth and development of the fetus. In cases where fetuses are imminent to termination, the researcher does not have obligations to protect fetal interests and the fetus is not a participant.

The co-participants model for fetal participation is one that can be easily applied to the TCPS2's current structure and goals, clarifies the role of the parent and fetus in studies with various levels of fetal and parental involvement, and can increase the ability for prospective participants to make informed decisions that are in the best interests of themselves and their fetuses. By using a general definition of participation that does not rely on personhood, the co-participants model ensures that the research status of the fetus does not infringe on the pregnant parent's autonomy while still ensuring that fetal interests are adequately protected.

Acknowledgements

I would like to acknowledge that this work could not have been possible without the kind assistance of the AIDS Clinical Trial Group and International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) network who provided me with the copies of the trial consent forms that I have referenced in this paper.

I send many thanks to the philosophy department at the University of Waterloo for their support in getting me to this point, even after I moved across the country. This includes my supervisor Dr. Matt Doucet and my other committee members Drs. Katy Fulfer and Patricia Marino, as well as Drs. Carla Fehr and Chris Lowry who were always looking out for my best interests. Thanks also go out to my family; including those who have passed and those who are not yet born, but especially my husband Jorge Sanchez Perez without whom I may have never pursued a PhD.

Finally, I could not have completed this task without taking advantage of the privileges that I have as a middle-class white woman in Canada where I benefit every day from the unjust oppression of others nearby and worldwide. Although I work to change this situation, I cannot ignore that I do still contribute to it.

Dedication

This dissertation is dedicated to my child Valentina. You kept me focused on what was important and motivated me to finish my work by just being yourself.

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List of Abbreviations

ACTG – AIDS Clinical Trial Group

AIDS – acquired immunodeficiency syndrome

APA – American Psychological Association

CBPR – community-based participatory research

CIHR –The Canadian Institutes of Health Research

CIOMS – Council for International Organizations of Medical Sciences

CRC – Convention on the Rights of the Child

FDA – Food and Drug Administration

HIV – human immunodeficiency viruses

ICLAS – The International Council for Laboratory Animal Science

IMPAACT – International Maternal Pediatric Adolescent AIDS Clinical Trials Group

LMP – last menstrual period

MTCT – Mother-to-child transmission

NSERC – Natural Sciences and Engineering Research Council of Canada

SDM – substitute decision maker

SSHRC – Social Sciences and Humanities Research Council of Canada

TCPS2 – Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans

UN – United Nations

WHO – World Health Organization

WMA – World Medical Association

Introduction

There is a current lack of research during pregnancy, which is harmful for both pregnant parent and fetus, and of course the subsequent child. This lack is mostly seen for studies that are not centered around pregnancy itself, such as testing safety and effectiveness of medications for mental illnesses taken during pregnancy. In 2008, Lyerly and colleagues sounded the alarm that only twelve medications have been approved by the United States Food and Drug Administration (FDA) for use during pregnancy and that all of them were for pregnancy-related issues (p. 7). This is despite the fact that chronic illnesses such as diabetes and hypertension affect four percent of pregnancies each, with hundreds of thousands of pregnant people being affected by psychiatric illnesses, cancer, and autoimmune diseases (Lyerly et al., 2008, p. 6). In 2024 in Canada, we cannot be said to be much better with Health Link BC advising residents of British Columbia that medications that are considered safe in pregnancy are often not studied in clinical trials, but rather have been taken in practice so long that doctors “usually” call them safe (Health Link BC, 2024).

One reason for a lack of research is due to hesitancy by Research Ethics Boards (REBs) to approve research during pregnancy (Langston, 2016, p. 39), and hesitancy from researchers to even develop studies and apply for approval. At the base of this hesitation is a lack of clarity about whose risks, benefits, interests, and wellbeing are central to the research. As it currently stands, fetuses are not considered participants of clinical research in Canada, but their wellbeing and development is required by the latest Tri-Council Policy Statement (TCPS2) guidelines to be considered and protected by researchers. This is a difficult line to walk. As Wild and Biller-Andorno (2016) put it, “for the discussion of how to include pregnant women

in clinical research, and especially how to assess possible risks, clarity on who is the research participant is crucial” (p. 130).

Although my focus will be on the Canadian context, there is a concerning implication from the United States that can help demonstrate why this discussion is needed. From 1991-1993 the AIDS Clinical Trial Group (ACTG) performed clinical research on a new medication called zidovudine in order to test its efficacy in preventing parent-to-child transmission (MTCT) of human immunodeficiency viruses (HIV) during pregnancy, childbirth, and breastfeeding. The original study was called ACTG 076 and in the consent forms graciously provided to me by The International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT), there is mention of the “mother,” “father,” and the “baby” where the mother and baby are participants of research, and the father is sought out to provide consent for the baby to participate in addition to the mother. Since the research begins during the prenatal period and requires follow-through after birth, if fathers are present and unwilling to consent to their “baby” participating in the study, then consent is considered to not be obtained and the pregnant parent is not entered into the study.

Currently, the FDA recommends that the father’s consent must be sought in cases where the fetus is central to the research goals, meaning consent forms like the ones in ACTG 076 could appear again. The FDA makes exceptions for cases of conception through sexual assault or incest and therefore does not always require a “father’s” consent to perform the research, but researchers must make an attempt to find a father and seek their consent when available (U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, 2018, p. 5).

This case brings up many ethical and legal questions about what it means to be a participant in research for a fetus and what role consent plays. It is true that, once the child is born, it would be important to consider both parents' willingness for their child to participate in research, but in the Canadian context, it is not required that all parents or guardians be asked to provide consent. It is also true that the trial requires a follow-up with born children, so ensuring consent is obtained for that portion of the trial before the research begins is also an important step. However, there are no clear guidelines in the United States, one place where this trial took place, or in Canada, on whether a fetus is a participant of research and if their consent is required by proxy of a parent or guardian.

This creates a dilemma in how pregnant people and their fetuses are treated in research. By requiring a "father's" consent for the fetus before the trial begins, this study implied one of two things. 1) That fetuses are participants of research and require proxy consent from both parents in order to participate in research, or 2) that fetuses are not participants of research but pregnant people require permission from the person labelled as their fetus' father in order to participate in research. Neither of these implications is desirable. 1) is undesirable mostly because this is not an explicit feature of Western clinical research guidelines. Fetuses are not stated to be individual participants separate from their pregnant parent, and proxy consent for their inclusion is not required. If implication 1) is correct, then the guidelines need to catch up with the fact that fetuses are participants and begin to discuss all the details surrounding their inclusion, like whether both parents are needed to provide consent.

Implication 2) is also undesirable because it places pregnant people in a separate category from all other autonomous adults. Under no other circumstances would an adult who is capable

of consenting for themselves be required to seek permission from another adult to participate in research. I function under the assumption that the ACTG 076 researchers, following FDA recommendations, were not intending to produce either of these implications, but more strongly was not intending to suggest that pregnant people require special permission to participate in research. This brings us to the question of *can fetuses be participants?* and if so, *what ethical principles and should guide this status?* This is where my work comes in. You may be thinking “but 1993 was 20 years ago! Surely, we have an answer to this question by now” and you’d be wrong. It was over 30 years ago, but also, no, we do not have an answer to this question.

Currently, the TCPS2 is the overarching set of guidelines for most clinical research with human participants in Canada. We can see in these guidelines that the confusion about the status of the fetus persists. Fetuses, as well as fetal tissue and embryos, are categorized as “human biological material” alongside blood, tissue, organs, and other samples Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, & Social Sciences and Humanities Research Council of Canada, 2022, p. 13). However, within the TCPS2 guidelines, there is a clear separation between the treatment of blood, tissue and organs, and the treatment of fetuses or embryos. Most notably, biological materials like blood have a section in the guidelines mentioning the importance of their proper preservation and disposal in a safe and confidential manner, whereas guidelines about fetuses emphasize the importance of minimizing risk and maintaining the wellbeing of the fetus.

It is clear, then, that even with guidelines updated as recently as 2022, here in Canada, we have placed fetuses under this same quasi-participant status. This quasi status means the fetus’

individuality is not recognized, but their vulnerability and wellbeing are. Although there is no encouragement to find the fetus' "father" to request consent under the TCPS2, there is a distinction pertaining to the goals of research involving fetuses and the goals of research involving biopsied tissue. Furthermore, the TCPS2 includes fetal tissue and embryos in the same category of protection as fetuses, despite the goals of research involving something like fetal tissue differing from that of a whole fetus. The goal in my work is to focus on the role status of the fetus – which is the being beyond 57 days of gestation – and does not consider the status of an embryo, blastocyst, or zygote.

A Brief Note on Me

I stumbled upon this topic in my Masters. Even as an undergraduate, I was interested in the ACTG 076 case and at first my interests grew from there as I learned more about the case and the ethical questions and concepts that arose. Throughout my Masters, I would occasionally wonder if I was speaking from a place of ignorance. Of course, there will always be some level of ignorance in anyone's work, but I felt that my inexperience with medical research and pregnancy made me vulnerable to important challenges I would not be able to address. Well, not too long after finally committing to continuing this topic for my PhD dissertation, I learned I was pregnant for the first time and I have to say, the experience made no difference in my connection to the topic. The only thing that may have changed is that occasionally I would find it difficult to read cold statistics about "fetal death" without thinking about my child.

My passion for this topic comes from my love of puzzles and my desire to find answers to important questions that no one seems to want to touch. The status of a fetus is an extremely

loaded topic in bioethics, and I ploughed into this fully aware that I would either receive very strong opinions or be met with refusal to engage. I am forever grateful to my committee for being willing to take this on and put their faith in me that I would be able to handle this question with the proper care and academic rigor that it deserves. I just hope that I have not let them down.

Clinical Research

The distinction between medical research, clinical research, and non-clinical research is not always agreed upon. In general, clinical research is performed on humans and includes research aimed to test medications, diagnostic or screening tests, and outcomes related to clinical practice. It will sometimes involve tissue sampling, imaging, exercise regimes, and consuming medications. Non-clinical research is any research that falls outside of this scope. For human research, this can include collection of personal or demographic information.

Clinical research is split into five main groups: preclinical trials, and Phases I-IV. Pre-clinical trials include non-human animal research and studies of human cells or tissue, then Phase I is a smaller group of healthy volunteers in order to test the safety of the intervention in question that has shown to be safe in preclinical testing (Grady et al., 2013, p. 158). For example, if a pain medication with a new active ingredient is going to be tested at Phase I, people who do not require pain relief will be given small doses of the medication or the ingredient to see if they develop uncomfortable or harmful side effects. Phase I can also be useful to test different dosages.

Phase II are smaller sub-groups that test a range of doses, potencies, and compositions of the intervention in question in order to determine an optimal dosage or regimen. This time the

volunteers would need pain treatment would take the entire medication, not just the one ingredient. For instance, some might be given 100mg once a day, while others would be given 10mg 3 times a day, and the results would be compared to prepare for the next phase. Phase III tests the optimal dose or regimen of the intervention on a relatively large group (Grady et al., 2013, p. 158). So, if it was found in Phase II that 10mg 3 times a day produced more efficacious pain relief with the lowest amount of side effects, that is what all volunteers would be given in the active arm of Phase III.

Phase III is often anonymized, which means the participants do not know if they are receiving the intervention in question or a control; like a placebo or an already-approved pain medication. This can also include double-anonymized trials where even the researchers are unaware which intervention the participant is receiving. Phase III is what many people imagine when they think of clinical trials that test the efficacy of an intervention and will be the bulk of my discussions. Phase III trials are also what is required for interventions to be approved by relevant regulating boards. Finally, Phase IV tests what is known as the effectiveness of the intervention, which is the outcome for common usage, these studies are often performed after the intervention has been approved for the market and their common usage can be observed (Grady et al., 2013, pp. 158-9).

Condoms are a good example to understand the difference between efficacy and effectiveness. One might often hear that condoms are over 98% efficacious at preventing pregnancy with perfect use and closer to 87% effective with common usage (Planned Parenthood, 2024). The difference here is that not everyone uses condoms perfectly, so it becomes important to know the difference between perfect use under ideal clinical settings,

and common use in everyday life. Phase III tells us perfect use efficacy and Phase IV tells us common use effectiveness, which is why Phase IV is a much larger observational study performed after the intervention is available on the market.

My aim in this work is to look at the guidelines and policies for the clinical research context, and especially of that in Canada. I will be drawing upon some literature that focuses on medical practice, or non-clinical research settings and I will also be formulating my own examples that consider these contexts. These are all for illustrative purposes to either contrast these contexts with clinical research settings, or to show potential implications on the extremities of clinical research. Throughout, I will also be drawing upon a series of work from Laurence B. McCullough, Frank A. Chervenak, and occasionally other co-authors. These two authors in particular have championed the concept of a “fetus as a patient” in the context of clinical practice and applied the concept in some ways to clinical research, but I agree with criticisms by Lyerly et al. (2011) and find that their view heavily relies on particularities of clinical practice that make it difficult to map cleanly onto the research context. These issues will be discussed in more detail in Chapters 2. For now, it is important to note that most clinical research does not have the aim or probability of providing beneficial treatment for those involved. McCullough and Chervenak (1994) state that an individual is a patient when they are “(1) presented to a physician (2) for the purpose of applying clinical interventions that are reliably expected to protect and promote the interests of that individual” (p. 104) and this cannot help us capture what it means to be a participant for the general population or for fetuses.

It is also important to note that the aims of research are different than the aims of treatment.

Throughout the work, I will be discussing “benefits” of clinical research, but these benefits are not the same as the benefits one can expect from therapeutic treatment from a physician. This is especially true in Phases I and II where research participation cannot directly benefit the research participant (Lyerly et al., 2011, p. 50), since the aims of these phases are to answer specific questions about safety and effects of the intervention and are not aimed at seeking efficacious treatment for a condition the participant has.

For participants of Phase III trials, some direct benefits might occur if the intervention they are taking proves to be beneficial to the condition they have. However, this is not guaranteed since the goal of the research is to answer the question of whether the intervention is beneficial, so its efficacy is not known beforehand. This concept is known as clinical equipoise and is recommended as a “starting point” for research design under the TCPS2 (Canadian Institutes of Health Research et al., 2022, p. 199), leaving room for contexts in which equipoise proves to be less useful, but still holding it as a basic value of research. Furthermore, because many of the participants will be administered a control, which in some cases is a placebo, participant benefit is not guaranteed. Participants who receive an active control in some research contexts could benefit from this access to an intervention they might not otherwise have, but since the intervention is available and access outside of research should be a goal we all strive for, this cannot be seen as a direct benefit of research participation in general.

Overview

This dissertation has six chapters. Chapter 1: The Road So Far sets the stage for where we are currently with the status of the fetus in research and gives a more in-depth explanation for

why my work is needed. I show that there are two main reasons for the historical exclusion of pregnant people in clinical research that have led us to 2024 without a clear answer. The first is a desire for “clean data” and an exclusion of pregnant people de facto through an exclusion of nearly all women and usually anyone assigned female at birth (AFAB) from most medical research. The second is a focus on the vulnerability of pregnancy and fetuses and a belief that vulnerability requires exclusion from research as the sole form of protection.

As it pertains to the current exclusion of pregnant people from research, there is reason to believe that without a clear answer to the status of the fetus in research, REBs are hesitant to approve various research projects that would involve pregnant participants, as well as researchers hesitant to pursue them. There is good reason for this, including pregnant people in clinical research is not as simple as recruiting them for studies designed outside of the question of pregnancy. This hesitancy, therefore, can be related to the concern that fetal wellbeing is sometimes central to the research question, but the pregnant parent is considered the only participant of the research, leaving questions about how to handle a balance of potential competing interests, and a concern for fetal welfare when the pregnant parent’s health outcomes are central to the research question. It then follows that, if we answer the question of the status of the fetus in research, we can develop guidelines that reflect this status and reduce the hesitancy to seek out or approve research projects.

Chapter 2: Focusing Our Vision addresses the question of “what does it mean to be a participant?” and examines the different ways in which one can be involved in research. I conclude that there are three main types of data analysis that can determine one’s level of involvement and each type can either include awareness of the research in question or a lack

of awareness. Based on how the terms are used in common literature, and the justifications behind the switch to the term “participant” over “subject” in many cases, I present the following definitions: A subject is a being who is unintentionally involved in a research project where their data is analyzed for the purposes of research outcomes; where as a participant is a being who is knowingly and intentionally involved in a research project where their data is analyzed for the purposes of research outcomes. This does not require the more stringent declaration intentionality of legal consent.

By establishing a general definition of subject and participant in research, Chapter 2 begins the first step of determining whether fetuses can be participants in some research depending on how they fit these definitions. This step not only helps to conceptually define what it means to be a participant, but also allows us to map this concept onto the TCPS2 that governs much of the research on humans conducted in Canada. By ensuring we examine what it means to be involved in research in different ways, we can use these definitions in Chapter 4 to see what principles surround the inclusion of non-fetal subjects and participants and which of these can apply to fetal subjects.

Chapter 3 answers my first central question of *can fetuses be regarded as participants in clinical research?* and the two sub-questions that come from it: Can fetuses *ever* be regarded as participants in clinical research? and can fetuses *always* be regarded as participants in clinical research? I do this by introducing four example cases of potential clinical research that could occur involving pregnant people and assess the level of involvement for both the pregnant parent and the fetus: (1) *Eye Drops*, (2) *Insulin*, (3) *Non-Invasive Prenatal Testing (NIPT)*, and (4) *human immunodeficiency viruses (HIV)*. Looking at the type of data analysis

determines whether they are a subject, participant, or neither in each case. Based on my previous conceptual definition of participant, it becomes clear that a fetus is never a participant of research due to their inability to intentionally involve themselves, but still can be a subject, and should be considered as such in some relevant cases. However, we will see in Chapter 5, that when applying the conceptual definition of subject to the TCPS2, both subjects and participants are labelled as participants in these guidelines.

Chapter 4 then goes on to answer the second central question of *assuming fetuses can be regarded as participants in at least some clinical research, what ethical principles should guide this treatment?* While only focusing on ethical principles, Chapter 4 argues that it is consistent within the current Canadian guidelines to require proxy consent for fetuses in at least some research where the fetus is a conceptual subject. I recommend that this requirement be used mostly in cases where the addition of proxy consent can provide benefits to both fetus and pregnant parent through clarity about the role of each in the research and their individual risks.

Chapter 5 builds on the principles of Chapter 4 to develop policy. Specifically, I make direct and detailed suggestions for changes that can be made to the TCPS2 in order to properly treat fetuses as subjects in the appropriate research settings. The TCPS2 does not use the term “subject” nor distinguish the conceptual difference between a subject and a participant, so it is here that I switch to calling fetuses participants for the sake of the policy. My main recommendation is that fetuses not imminent to termination should be considered participants under the TCPS2 in addition to born humans, and that fetuses imminent to termination, or already deceased, can remain under the category of “human biological materials” with no other

changes to the guidelines for that category.

Chapter 5 is also where I develop what I call the “co-participants model” for incorporating pregnant people and their fetuses into research as two participants where appropriate. The co-participants model states that the pregnant person and the fetus are individual participants whose interests differ and are sometimes at odds. The co-participants may both require individual consent, but since they are inextricably linked, it is necessary to ensure that their participation and health outcomes are regarded in relation to one another. The benefit of the co-participants model over other proposed models is that it is able to capture the general case of what it means to be a participant without relying on personhood or capacity arguments. This is consistent with the TCPS2 handling of participants and, therefore, is an appropriate model for the guidelines to implement.

Finally, Chapter 6 addresses concerns about the implications of providing fetuses a participant status and some objections that come from these. This is where I address the looming question of abortion and how elevating the status of a fetus to that of a subject of research, and recommending proxy consent for their inclusion should not have any bearing on medical treatment such as a dilation and evacuation for miscarriages or terminated fetuses. Since the status of a fetus as a subject does not rely on a concept of personhood, there is no implication in my work that the status of a fetus has changed outside of the research context.

The overall goal of this work is to find clarity about the role of the fetal participant and make suggestions for how this newly considered role can be implemented in Canadian research to hopefully reduce hesitancy from researchers and REBs and also ensure that pregnant parents and fetuses have adequate consideration for their interests and wellbeing.

Chapter 1- The Road So Far

“Pregnant women get sick, and sick women get pregnant” – Francoise Baylis¹

Introduction

It is no accident that we are two decades into the 21st century without a clear answer on how to treat fetuses in human research. The first central question of my project is: *can fetuses be participants?* and historically in research they have not been included as such. Not only because there is little research involving pregnant people, but also because the research that does involve them does not often treat their fetuses as individuals separate from the parent and requiring some sort of proxy consent. However, as we have seen in the Introduction, occasionally fetuses are implied to be participants and there have been suggestions by some that this should become more commonplace. This leaves the status of the fetus in research unclear.

The status of the fetus as a participant is not clear because the foundation on which it is built still has wet cement. What I mean by this is that, until very recently, pregnant people were the ones without a clear position in research. There are two main overlapping reasons for this that look different in a historical context to today. Reason 1) is a desire for “clean data” or scientific rigor that comes from more homogenous study samples. This historically included an overall exclusion of anyone who was assigned female at birth (AFAB), and currently only excluded pregnant people. Reason 2) is a desire to protect “vulnerable groups,” including pregnant people and their fetuses, from harms. This began with an FDA ban in 1977 on excluding almost

¹ Baylis, F. (2010) “Pregnant women deserve better” *Nature*, 465. 689–690

all people who are AFAB due to their potential to become pregnant, and with changes in 1994 only applying to people who were already pregnant (McCarthy, 1994, p. 695; Mazure & Jones, 2015, p. 1). Canadian practices followed a similar pattern.

Within the current use of reason 2) there are diverse motivations and implications underlying the labelling of pregnant people and their fetuses as vulnerable which include a) fear of harms that might come when researchers exploit their participants, b) concerns about competing interests between the pregnant person and their fetus leading to ethical impasses, and c) ingrained misogyny that motivates the desire to protect fetuses from harms that their parent might cause by making poor or irrational decisions while pregnant. Reasons 1) and 2) for exclusion and their sub-motivations have caused many complications for research during pregnancy in the history of Western research. By excluding nearly all women and all pregnant people for decades, it has been difficult to begin their responsible inclusion over the last few years and help pregnant people and their fetuses benefit from this research. Without a robust set of guidelines backed by strong theoretical work, pregnant people continue to be left behind when science progresses. It should be clear, then, that taking a closer look at the role the fetus plays in all of this was not always the first priority of policy makers.

Thankfully, where we are situated now in 2024 has been a great step towards fair and responsible inclusion of all of these groups and much progress has been made. To map out the road so far, this chapter has eight sections. 1.1 takes us through the historical exclusion of pregnant people, and marginalized groups more generally, looking at how reasons 1) and 2) played out through harms created by exploitative studies and how that developed a motivation to protect groups that were seen as vulnerable, such as pregnant people. This gives a basic

explanation for why pregnant people do not have a clear position in research. The focus in this section is on previous practices based on ethics guidelines and policy that often excluded all women and anyone thought to have a fertile uterus. These practices are no longer followed but explain the path of current policy and why it might still exclude pregnant participants.

Sections 1.2-1.3 cover more recent examples of 1) “complexity” and 2a) the first motivation for vulnerability that came from policy recommendations, researchers, and bioethicists where *de facto* or systemic exclusion of pregnant participants still occurs. Sections 1.4-1.5 also answer the question of why there is still a current issue with the exclusion of pregnant people and how these exclusions linger despite the concerns being addressed. The underlying motivations of 2b)-2c) are looked at in detail as well as three different concepts of vulnerability that often get conflated.

Next, 1.6 introduces the concepts of autonomy and justice to explain why a focus on vulnerability and a blanket exclusion of pregnant participants is now considered unethical. Section 1.7 moves on to the responsible inclusion of pregnant people by presenting arguments from bioethicists about possible steps forward for principles, guidelines, and policy to adequately include pregnant people in research. Finally, section 1.8 focuses on patient and participant perspectives from pregnant people, or people who have recently been pregnant, about their desire to be included in research and their willingness to participate in a variety of studies. Overall, this chapter leads to the conclusion that the current debate has set up the question of *can fetuses be participants?* without ever answering it, pointing to the need for my work to fill in this gap.

1.1 Historical Exclusion

The history of the inclusion of pregnant people, and women more broadly in medical research in the United States and Western world is complicated. For decades, research was not well regarded by the general public. Research was seen primarily as a predatory practice and for good reason, since there was much evidence of exploitative studies (McCarthy, 1993, p. 696). However, this view began to lighten as more protections were put in to ensure that participants were not mistreated. After the harmful Nazi experimentation during World War II, the Nuremberg Code was created in the 1940s and meant to be adopted broadly. Later and more locally to the US, the FDA established protections for research in the late 1960s (McCarthy, 1993, p. 695). After strict enforcement and punishment for those who violated the protections against harm and exploitation in research, the 1980s saw a shift in the public perception of research participation, research was seen as an important scientific undertaking in general and “an attractive way to receive inexpensive health care” for those who participated (McCarthy, 1993, p. 695).

As mentioned above, reason 1) for the exclusion of pregnant people is the desire to have “clean data” or results that can be easily verified and replicated. What this means is that the more homogenous the sample group under study is, the less likely that factors such as social or genetic difference can cause interventions to look more or less efficacious than they might otherwise be. For example, if one is testing the efficacy of a sleep aid, using a broad sample of the population that includes people who work night shifts, and those with diagnosed insomnia might make the sleep aid appear less efficacious than if it were solely to be tested on people who generally wake with the sun and only have occasional, rather than chronic, sleep

difficulties. In this case, the researchers would only test the sleep aid on this smaller subgroup of the population so they can ensure health concerns like insomnia, which are not meant to be treated by the aid, are not making the medication appear ineffective.

The application this has to most women, people who are AFAB, and pregnant people is that often physical diversity between sexes, hormone fluctuations due to menstrual cycles, and physical changes due to pregnancy would create the same concerns for researchers about the data and results as those who have complicated health concerns or uncommon sleeping habits, despite women making up approximately 50% of the population. In this case, the exclusion of pregnant people was not necessarily targeted at their pregnancy, but rather their ability to become pregnant, which was mostly determined by the fact that they had a uterus.

One might ask why it is a problem that some groups are excluded from research. As I will expand on later in section 1.6 and the discussion of justice, since different groups tend to have different health needs, a lack of research on one group, such as women, means a lack of information about health conditions and treatment that affect women in particular, or affect women differently than other genders. Research provides a benefit to the community by improving health knowledge and affecting healthcare and if there are members of the community who are excluded from participating in the research, they are excluded from the potential benefits of the research results.

Reason 2) for the historical exclusion of pregnant people more explicitly was a targeted exclusion of pregnant people and anyone who could become pregnant due to protection of their and their fetus' "vulnerability" to harms from pharmaceuticals or historically exploitative research practices.

Perhaps one of the most infamous examples of exploitative research practices in the Western world is that of the Tuskegee syphilis study which was not related to pregnancy. In this study, the US Public Health Service recruited Black men to test the progression of syphilis. The “participants” of the trial were often not told they had syphilis, that they were in a study, or that a treatment of their condition was available, resulting in hundreds of preventable deaths (Gaskin, 1997, p. 32). This study continued from 1932 until 1972 when it was finally put to an end after an Associated Press article exposed these issues (Gaskin, 1997, p. 32). Because of harms like these, protection from research became an important element for vulnerable groups and led to the exclusion of many people from participation for a long time (Liu & Dipietro Mager, 2016, p. 2).

Although it was not a harm that came about because of research, the thalidomide case was an example of harm caused by pharmaceuticals and affected the relationship between pregnancy and research. Thalidomide was a medication used in sedatives as a sleep aid, and to treat morning sickness in pregnancy (Langston, 2016, p. 34). It was never approved by the FDA in the United States before the effects on fetuses became known. However, it was used throughout Europe and Canada for a few years before being removed from the market (Langston, 2016, p. 34), although it is now available again for other uses around the world. The effect it had on fetuses was quite significant, ranging from disabilities such as deafness or limb difference (Franks et al., 2004, p. 1802) to severe harms such as organ defects and death (Miller, 1991, pp. 630, 659).

Despite being claimed to show no toxic effects in animal testing and no major side effects in a range of adults in clinical trials, thalidomide caused a significant number of miscarriages,

interfered with physical development in approximately 10,000 live births – many of them also resulting in childhood deaths – and caused numbness in the extremities of thousands of pregnant people (Langston, 2016, pp. 34-5). Most popular in Germany, the thalidomide case became a “wakeup call” about the effect pharmaceuticals could have on the fetus during pregnancy and heavily shaped the fear and caution that Europeans, Canadians, and many others have when it comes to consumption during pregnancy (Langston, 2016, p. 33).

Due to the potential harm a fetus could face and a lack of benefit from Phase I trials, the FDA effectively banned *all women* from Phase I trials in order to protect against harm to fetuses that could occur (McCarthy, 1993, p. 697). This 1977 guideline excluded “women of child-bearing potential” which included any pre-menopausal, and occasionally also post-menopausal cis woman. The guideline also excluded women who were using contraceptives, or with sterile partners and was not lifted until 1993 (Liu & Dipietro Mager, 2016, p. 3).

McCarthy points out the shift of the social view of research in the United States that happened in the 1980s due to a few factors including the raised assurance that research was being conducted ethically and the vast increase in health care costs that led many to see research participation as an affordable option for medical care (1993, p. 697). At this time, women and other designated vulnerable groups were slowly being accepted as research participants, but pregnant people were still left out due to reasons 1) and 2) – fluctuating hormone levels were seen as confounding variables to research, and there were continuing concerns about fetal safety (Liu & Dipietro Mager, 2016, p. 2).

1.2 Complexity and Exclusion

Reason 1) when it comes to more recent exclusion of pregnant people applies directly to the

complexity of the pregnant body, rather than a more general view applying to uteruses and the hormones associated with them. Even with the inclusion of many women, pregnant people remained excluded for their more particular different needs within the group. So, we can see that first pregnant people were excluded mainly for having uteruses or being mostly women, then when women were more readily included, pregnant people were excluded again for being pregnant.

One way of framing this need for clean data is describing pregnant people as having a “physiological complexity,” and needs that make studies difficult to be both well done and cost effective (van der Zande et al., 2016, p. 70). The reason for this is that many Phase III clinical studies require a large portion of the population to ensure the data is enough to draw significant conclusions. Since pregnant people make up a relatively small portion of the population at any time, and since the nature of pregnancy means participants need to be recruited quite quickly upon finding out they are pregnant, there are logistical concerns with studies involving pregnant people that are not likely to occur with non-pregnant people.

For example, if researchers wish to study the efficacy of a new anti-nausea medication in pregnancy, they might choose to look for study participants in the Lower Mainland of British Columbia. Nausea is often strongest between 6-12 weeks of pregnancy, although many experience it earlier or later. This is a time when many people do not yet know they are pregnant, and even if they are aware, they do not have frequent prenatal care. Reaching enough pregnant people in such a large area will take extra time and resources, and it can be difficult to find people early enough in their pregnancy to contact the researchers, learn about the study, consider their desire to participate, consent to participate, and begin the intervention before

their nausea naturally subsides or they give birth.

If the researchers were simply testing the efficacy of an anti-nausea medication in the general population, they would perhaps be able to limit their area to the city of Vancouver, which is over 100x smaller in land mass, since they now have access to the entire population rather than just a small percentage. They could conduct the study in a shorter amount of time because once they recruit participants to the study, they do not have the same need to recruit more participants after some “graduate” and give birth. Since they can limit the physical area and time of the study, fewer resources would be needed to recruit participants and conduct the research, bringing down costs. Finally, whether pregnant participants are included as the entire sample population or a stratified group, there would still need to be a significant number of them involved in the research, meaning the study of the general population would provide results for nearly everyone for likely a lower cost than the pregnancy study that only provides results for the pregnant population.

By needing to stratify pregnant people into a separate group, either during the initial study, or as a secondary study to find new results, the motivation to continue research on pregnant populations decreases for any intervention or illness that is commonly experienced outside of pregnancy. Researchers focused on determining the effectiveness of a particular intervention will reasonably want to ensure that they have results for non-pregnant people first since at any point in time the percentage of the population that is pregnant is relatively low. Testing the intervention on pregnant populations can come later, but that research often does not happen due to the other concerns about vulnerability, competing interests, and misogyny that we will see in sections 1.3-1.5.

The goal of having “clean” data that can be generalized or extrapolated to a large portion of the population runs through the whole timeline of exclusion of pregnant people. The more homogenous the participant population, the more researchers can control for various confounding factors. If your research involves the “healthiest” or “most neutral” of the population – often manifested as young white men – then you get the best results that can be applied to the entirety of the rest. In the past, when research was conducted on homogenous groups, the results were then extrapolated to the general population. We learned, however, that physiological differences matter in many cases of medical practice. Pharmaceutical choices cannot be made simply by finding the most effective method for a group of men, then adjusting for a lighter dosage for women and children. Hormonal and growth differences between demographics might mean that some medications are unsafe at any dose for children, or ineffective for many women (Lyerly et al., 2008, p. 9), especially during pregnancy (Constantine et al., 2020, p. 26).

For example, the way pregnant people metabolize medications such as amoxicillin is different than their non-pregnant counterparts and it was discovered in 2007 that the level of amoxicillin necessary to treat exposure to anthrax might not be possible to achieve in pregnant people despite amoxicillin being considered the standard of care treatment for non-pregnant people (Lyerly et al., 2008, p. 9). Although these physiological differences are exactly what requires pregnant patients to be in need of their own subset of research, they end up being a reason to justify their exclusion in many studies that are not specifically aimed at pregnant people themselves. Having multiple participant groups each with their own needs and outcomes makes a study logistically complex and more expensive than simply biting the bullet

and drawing conclusions only about non-pregnant demographics.

1.3 Vulnerability and Exclusion

Recall that reason 2) is that researchers and policy makers often label both the fetus and the pregnant parent as vulnerable groups, and there are three main reasons in which both groups continue to be systematically excluded from research: a) fear of harms that might come when researchers exploit their participants, b) concerns about competing interests between the pregnant person and their fetus leading to ethical impasses, and c) ingrained misogyny that motivates the desire to protect fetuses from harms that their parent might cause by making poor or irrational decisions while pregnant.

Although there had been a shift throughout the 20th century from viewing all research as exploitative and harmful to viewing research as a public good that could potentially provide benefit for the participants, it remains important to recognize that research does expose participants to risks of harm that they might otherwise easily avoid. Due to this, minimizing risk in research to all participants but especially vulnerable groups, remains a goal. With the more recent attitude that all groups should be able to benefit from research as well, a blanket exclusion of groups labeled as vulnerable is no longer considered a justifiable step to minimize risk, however systemic exclusion of these groups continue. This speaks to 2a) or the continued exclusion of pregnant people from research due to the fear that researchers might cause them harm through exploitative research practices.

One major issue that arises when it comes to intentional blanket exclusion, or *de facto* incidental exclusion of groups who are labelled as vulnerable is the lack of a shared definition of vulnerability. Even in more recent literature and guidelines, vulnerability has been defined

as a susceptibility to harm (Schwenzer, 2008, p. 1343, Ballantyne & Rogers, 2016, p. 141), diminished capacity to know or understand research (Park & Grayson, 2008, p. 1103), or simply not defined at all such as in the US Code of Federal Regulations (Schonfeld, 2013, p. 191). We will see in section 1.5 with the discussion of reason 2c) that this second concept of vulnerability being defined as diminished capacity has strong implications against pregnant people even if the definition is not accepted by all policy makers. Discussions of these definitions and interpretations of vulnerability show that pregnant people do not fit all concepts of vulnerability and, therefore, more care and attention should be taken when labelling them as vulnerable.

Separate from the concept of vulnerability is that of exploitation, which is taking unfair advantage of a vulnerability, but not all vulnerabilities automatically cause exploitation to occur (Ballantyne & Rogers, 2016, p. 146). The harms or wrongs of exploitation can be explained by two different accounts: unfair benefits and instrumental use. On the unfair benefits account, the exploitation is a moral wrong that occurs when party A receives an unfairly disproportionate benefit from the burdens of party B (Ballantyne & Rogers, 2016, p. 149). When it comes to research, a participant might be vulnerable to be exploited by researchers if the researchers stand to gain a lot of benefits from the study that the participants do not.

Recall that research is not meant to provide therapeutic benefits for the participant, so there are not always direct benefits to the research for the participant, but that does not mean that a participant does not benefit at all. It is possible for a participant to indirectly benefit from their participation from the medical advancements that are made within the community due to

the research. It is also the case that participants are often compensated for their participation in various ways, such as a small monetary sum or access to a specialty clinic that might otherwise not have room for them. This means that researchers have many ways in which they can ensure there is a balance of benefits between themselves and the participants so as not to exploit them.

The instrumental use account is a Kantian understanding of exploitation where the moral wrongness comes from treating one as mere means and cannot be mitigated by consent to be exploited (Ballantyne & Rogers, 2016, p. 149). On this account of exploitation, the focus would be on avoiding certain practices rather than trying to compensate for them by providing benefits to the participant. For example, it is often considered unethical to conduct research without a purpose or that has no scientific value such as using a placebo control when there is a proven effective medication that is already on the market. One could be exploited by these practices if researchers attempt to redo studies with known results in order to boost their publication numbers. In these cases, it does not matter if the participants are compensated for their burdens of being given a placebo for a condition that has a known treatment because doing so has no scientific value and would therefore be exploiting the participants by treating them as mere means to gain publications, rather than as humans who the suffering of being without needed medication.

When someone is labelled as vulnerable, there is the belief that they are more likely to be exploited in research, perhaps because they cannot advocate for themselves to ensure they are not overburdened or treated as mere means. However, vulnerability does not necessitate exploitation in research since it is possible to ensure benefits and burdens are balanced and

participants are treated with respect. This means that it is possible to conduct non-exploitative research on vulnerable groups and therefore there is more thought and care that needs to be taken to protect them from exploitation than simply excluding them completely (Ballantyne & Rogers, 2016, pp. 150-1).

Not only does vulnerability not necessitate exploitation, but in the particular case of pregnant people, there is less of a benefit that researchers can gain from the studies than with most non-pregnant people, meaning they are actually less likely to be exploited on the unfair benefits account (Ballantyne & Rogers, 2016, pp. 151-2). Since one justification for the exclusion of pregnant people, either in policy or practice, is the physical complexity or financial burden of including a separate sample group, pregnant people can be seen as a burden to researchers rather than a benefit, making them less prone to exploitation, and undermining the justification for excluding them due to vulnerability to exploitation.

In addition to a reduced vulnerability to exploitation, Ballantyne and Rogers suggest that the historical exclusion of pregnant people from clinical research is itself a vulnerability since they define vulnerability as capacity to be harmed and policies aimed at protecting pregnant people harm them further by taking away knowledge about safe treatment of medical concerns (Ballantyne & Rogers, 2016, p. 145).

Recall that, although research can pose risks to participants, it is also seen as a good that can provide benefits to the community and sometimes the participants. As we saw with the amoxicillin example, there is needed information about how medicines are metabolized different by pregnant people so adequate treatment can be provided. For concerns as serious as anthrax exposure, being excluded from research would mean having no recommended

course of action capable of saving one's life and potentially being unaware that this is the case. All this adds up to pregnant people being less vulnerable to exploitation by researchers than initially assumed as well as being more vulnerable to harms in medical practice when excluded from research.

For Ballantyne and Rogers (2016), vulnerability can be split these into three categories: inherent, situational, and pathogenic. They define vulnerability as “the capacity to suffer or be harmed” (Ballantyne & Rogers, 2016, p. 141), and, if we take a look at a pregnant person under this concept, we can see that they have all three, inherent, situational, and pathogenic vulnerabilities. First, inherent vulnerabilities are ones that we all have by virtue of being human beings. When it comes to pregnancy, your body changes, so the things you are inherently vulnerable to will also change, such as having lessened physical stamina or disorders like pre-eclampsia as well as psychological harms from these changes (Ballantyne & Rogers, 2016, pp. 143-4).

Situational vulnerabilities are external to us and are context-specific, which allows us to capture some differences between different persons and groups and the vulnerability they might face. For pregnancy, situations such as financial strain or a change in interpersonal relationships can make them situationally vulnerable when these concerns are not adequately addressed (Ballantyne & Rogers, 2016, p. 144). Thankfully, situational vulnerabilities can be significantly reduced by human action, choices, and support given to the people in the vulnerable situation (Ballantyne & Rogers, 2016, p. 144). Since situational vulnerabilities can be mitigated and reduced, Ballantyne and Rogers reject the practice of using these types of vulnerabilities to label one a “vulnerable group” and instead posit that we should be addressing

vulnerabilities based on their specific type.

Pathogenic vulnerabilities are a subset of situational vulnerabilities that can be categorized as “dysfunctional” such as situations of abuse, oppression, domination, or intentional harm (Ballantyne & Rogers, 2016, p. 145). It is likely clear here that research can make one situationally vulnerable by placing them in a situation where they might be harmed by participation and otherwise would not be faced with these risks. These types of situational vulnerabilities are often already addressed by common research guidelines that set out to protect participants from the potential harms they might face and ensure that they are actively choosing to participate with knowledge of the risks, rather than being situationally vulnerable against their will. It is for this reason that situational vulnerabilities are not sufficient to label a group “vulnerable”

Ballantyne and Rogers go on to point out that the historical exclusion of pregnant people in research causes a pathogenic vulnerability that needs to be rectified (Ballantyne & Rogers, 2016, p. 145). By using the term “vulnerability” to mean a multitude of factors, including a lack of capacity to consent, and by excluding pregnant people due to “vulnerabilities” without ever addressing where these might come in, or how situational vulnerabilities can be rectified, research practices have effectively treated pregnant people as incapable of making their own decisions about participation when the more apt vulnerability to address in research is pathogenic and their blanket exclusion leading to gaps in medical knowledge during pregnancy. Ballantyne and Rogers point out that most policies aimed at protecting the vulnerable do so with the assumption that vulnerable groups are unable to provide consent and do not stop to consider that this is not a fair attribution to pregnant people (Ballantyne &

Rogers, 2016, p. 145). As we will discuss further in 1.5, since most pregnant people are women, and it is misogynistic to assume without question that a large group of women cannot provide consent for their participation, the ongoing conflation of different vulnerability types adds to the misogynistic treatment of women, anyone AFAB, and pregnant people as incapable of rational decision making.

So far, I have been focusing on how the pregnant parent is labelled as vulnerable to research harms, but this goal of protection from harms is about both the vulnerability of pregnant parent and their fetus, which is often a strong justification for the exclusion of pregnant participants (McCarthy, 1993, p. 697). Fetuses have also previously been labelled as vulnerable groups in the US Code of Federal Regulations (Schewenzer, 2008, p. 1343). This is of particular importance to the first main question of my project: *can fetuses be participants?* By focusing on the potential harms to a fetus, considering fetuses a type of vulnerable group, and separating pregnant participants because of their fetus' vulnerability, rather than their own, fetuses are effectively being treated as any other vulnerable participant group. This leans in the direction of considering fetuses participants in research. The concept of participant will be thoroughly examined in Chapter 2.

1.4 Competing Interests and Exclusion

Moving on to 2b) the interests of the pregnant parent and their fetus in research might not always line up. This further complicates the ability to protect a vulnerable group while still including them in research since minimizing the risk to the parent might not minimize the risk to the fetus in the same way. For example, if we return to the thalidomide case, it is in strong interest of the pregnant parent to have a medication that treats both nausea and sleep concerns

during pregnancy. Without a medication like this, pregnancy could be even more harsh on the physical and mental wellbeing of the pregnant person. There is some interest that the fetus takes in this instance since reduced nausea means the pregnant parent will likely have an increased ability to consume adequate calories and nutrients that are needed for the fetus to thrive, but the likelihood of common nausea or sleep disturbances causing severe outcomes such as organ failure and death for the fetus is incredibly low compared to that of thalidomide.

In this instance, any research that is designed to test a new medication to treat nausea or sleep problems in pregnancy will have to weigh the interests of the pregnant parent in comparison to the interests of the fetus rather than seeing them as more closely aligned. It is fair here to call this a vulnerability in research since, under other circumstances, the goal would be to find a way to continue with the research while minimizing the risks and harms to the participant, but in this case, continuing with the research stands to greatly benefit the pregnant person while greatly risking the fetus, and simply avoiding the research stands to protect the fetus while causing the pregnant parent a lot of suffering. As we will explore more in section 1.5, Lucy Langston states that inaction is the most common choice for REBs (2016, p. 34), so even though inaction will cause suffering and still pose a small risk to the fetus that comes with untreated nausea, the desire for protection more often than not comes with a decision to do nothing at all.

1.5 Misogyny and Exclusion

Finally, 2c) is the ingrained misogyny that comes with a motivation to protect fetuses from harm that the pregnant parent (most likely their mother) could cause through their autonomous decision making. Misogyny is not always explicit, or even intentional and here it is mostly

seen as a failure to take a woman's autonomy into consideration, rather than a clear or direct accusation of irrationality or malice. Lucy Langston (2016) outlines one such way in which the desire for 2a), a protection of vulnerable groups from the harms of research, has resulted in 2c), the misogynistic outcome of grouping pregnant people and children together as "vulnerable populations" despite their vulnerabilities being distinct in nature.

Langston argues that the precautionary principle, when applied to pregnancy, has resulted in a stigma against pharmaceuticals taken by pregnant people due in large part to the harm that thalidomide caused for so many. As we have seen, this resulted in a complete exclusion of pregnant people, and most women, from research due to a preference for inaction. However, Langston shows that, at the same time as protections increased for pregnant people in research, they also increased for prisoners and children due to their being labeled as vulnerable groups. Langston is clear to separate pregnant people as being vulnerable due to the unique risks they face while pregnant, from the vulnerability that prisoners and children have due to diminished capacity for consent. For prisoners, this comes from the oppressive situation in which they live where their autonomy is actively being hindered on a daily basis, affecting their ability to seek medical help elsewhere or advocate for their own interests. For children, this is related to their cognitive development and a personal lack of capacity to understand the complexities of consent.

Constantly grouping pregnant people with children in discussions of vulnerability can imply that pregnant people have reduced capacity to give informed consent (Langston, 2016, p. 37). This is likely exacerbated by a lack of shared definition for who counts as vulnerable, and some even defining it as a diminished capacity. She attributes the ongoing hesitancy to

include pregnant people in research to this conflation, noting that it is important to ensure that the level of precaution taken to protect pregnant people and their fetuses from the harms of research does not result in their complete exclusion (Langston, 2016, p. 34).

Langston's concern here is that children through their vulnerabilities due to an underdeveloped mental capacity to consent, and incarcerated populations through their vulnerabilities due to a diminished capacity to exercise autonomy, are at a unique risk of exploitation that pregnant people do not face through their own vulnerabilities due to bodily changes such as metabolic differences or muscle weakness. In this way, Langston, and Ballantyne and Rogers are in agreement that it might not be wrong to call pregnant people vulnerable in research contexts, but that it is not useful to discuss vulnerable groups under the same umbrella, and it is harmful to treat all vulnerable groups as needing the same kinds of protection from research.

What we have here is a lingering *de facto* or systemic exclusion of pregnant people from medical research despite guidelines that request for their inclusion (Langston, 2016, pp. 37-8) and a rising belief that research involving pregnant people is needed because it provides more benefits than risks or harm. We have seen that this lingering concern comes from a desire to protect pregnant people and their fetuses from harms of research, because the competing interests that pregnant people and fetuses might face create logistic and ethical problems, and that there are misogynistic undertones that appear to accept treating pregnant people as irrational or non-autonomous rather than as complex.

In order to move forward from these concerns and begin to include pregnant people in research at a more reasonable and needed rate, we must first speak about the “non-

controversial” assumption that pregnant people can make informed decisions and that pregnant people care about the wellbeing of their fetuses (Kaposy, 2016, p. 52). Until recently, Western bioethics has allowed for implicit misogynistic assumptions to underly decision making about medical research by taking the decision about research participation away from pregnant people and excluding them entirely. As Kaposy puts it, there is an inconsistency between regarding pregnant people as autonomous beings who are capable of weighing risks to protect themselves and their fetuses, and automatically excluding pregnant people in order to protect their fetuses (Kaposy, 2016, p. 59).

Despite Kaposy positing this as non-controversial, it is still helpful here to present more empirical data from Germany that examined pregnant people’s ability to assess risks and benefits in research in light of the thalidomide case. One reason for this is that pregnant people might appear to have a diminished capacity for autonomy since pregnancy can put a higher pressure on them to protect their fetus above their own health. This pressure might lead pregnant people to be more likely to accept participation in research that is high-benefit, low-risk for the fetus (Wild & Biller-Andorno, 2016, p. 133). However, a simple change in one’s risk-assessment conclusion is not the same as a diminished autonomy and rather is an indication that the person is engaging in their rational capacities to properly assess the change in context of risk.

Wild and Biller-Andorno (2016) explain that “[i]n Germany, no European or national law explicitly regulates clinical research on pregnant women,” yet they remain excluded (p. 121). Like other jurisdictions, a fear of the harms to fetus by medication taken by the pregnant parent is one major reason why Germans might be hesitant to include pregnant participants despite

no national regulation against their inclusion. In addition, their exclusion is partially due to a concern from bioethicists that pregnancy negatively affects one's ability to properly assess risks (Wild & Biller-Andorno, 2016, p. 121). However, their research shows that pregnant people have equal risk assessment to non-pregnant people and considers added concerns that pregnant people have about risk to their fetus, such as harms similar to those caused by thalidomide, and personal desire to prioritize their fetus' health (Wild & Biller-Andorno, 2016, pp. 124-6).

As we have seen from Langston, the desire to protect pregnant people from the potential harms of exploitative research has led, at least in the case of the United States, to a lumping of all vulnerable groups into one, and a treatment of all vulnerable groups as having diminished capacity due to their vulnerability. It has taken some effort to tease apart these concerns over vulnerability to ensure that pregnant people are still protected from harms of research while also being treated as autonomous beings by default in part due to the competing definitions of vulnerability that sometimes rely on diminished capacity. Kaposy takes the stance of simply intuiting that pregnancy does not diminish one's autonomy, but Wild and Biller-Andorno take it one step further and show that although pregnant people may appear to be less-than-fully-rational due to their circumstances, their risk assessment simply takes their circumstances into account, which is why they make different decisions than non-pregnant people.

In addition to the concern about pregnant people being excluded from research, these perspectives on treating pregnancy as a vulnerability to exploitation in the same way we treat imprisonment or diminished autonomy point to a harmful undertone that ethics policies need to protect fetuses from their pregnant parents. In the context of historical misogyny, the

presentation of pregnant people, mostly women, as incapable of being adequate decision makers when facing these risks to themselves or their fetus perpetuates stereotypes of women as irrational or incapable. These stereotypes contribute to the harms that are created not only through the lack of participation in research, but in the message sent to the general society that pregnant people are unable to consent, or they pose a danger to their own fetuses.

Continued exclusion of pregnant people from all types of research does not clearly separate genuine concerns of physical complexity, competing interests, or research harms from assumed diminished capacity and irrationality. The problem is that all types of research, even ones where legitimate concerns can be addressed and rectified, still end up excluding pregnant people, which winds up treating them as incapable of making their own assessment of risks for themselves and their fetuses. It is important to be able to both ensure that pregnant people and their fetuses are not exposed to unnecessary harms of certain research settings, but also that pregnant people are treated with respect so that they can choose whether to participate in more moderated research.

1.6 Autonomy and Justice

In addition to the arguments that aim to negate previous views and assumptions about the vulnerability of pregnant participants, there are two main themes of positively supporting the need for their inclusion in research. The first of these is centered around autonomy or respect for the person. Autonomy is an important principle of bioethics that is featured as “central value within virtually all the leading approaches to health care ethics, feminist and other” (Sherwin, 1998, p. 19). Beyond the philosophical literature, autonomy is emphasized as important in Western research ethics guidelines. The TCPS2 used in Canada for research

ethics, focuses on the three principles of Respect for Persons, Concern for Welfare, and Justice (Canadian Institutes of Health Research et al., 2022, p. 6) Conceptions of autonomy can range from an emphasis on independence or self-sufficiency, to a relational approach that understands the self as a fluid and interconnected process (Sherwin, 1998, pp. 34-5). What they all share is the need to respect the choices one makes for oneself.

Within bioethics, the concern for autonomy results in an emphasis on securing consent. This is true for medical practice where the patient should be giving voluntary, informed consent to procedures, diagnostic methods, and treatment plans. In this case, consent is often secured by a conversation with the medical care provider about the medical concern, the procedure, and the treatment. In the context of research, the participant is not often benefiting from the research directly because they are doing something like undergoing a test or taking a medication with the purpose of providing information to the researchers about how that test or medication affects people. This distinction between treatment and research can become difficult to convey to patients who are prospective participants in a study related to their medical care, so in medical research, securing consent is seen as even more critical and it will often take the form of detailed conversations, information packages, and signing forms.

The bottom line in the autonomy argument in favour of inclusion is that a respect for autonomy means that autonomous adults get to consent for themselves. The act of excluding groups takes that option away, thus disrespecting their autonomy. Automatically excluding pregnant people in order to protect them or their fetuses undermines the autonomy of the pregnant person in these cases (Kaposy, 2016, p. 59).

The second positive argument in favour of the inclusion of pregnant people in research is

that of justice. As it pertains to research ethics, justice demands that people are given an appropriate opportunity to be protected from the harms of research and to benefit from its advantages, especially in comparison to others (Canadian Institutes of Health Research et al., 2022, p. 9). What this means is that no one person or group should disproportionately suffer the burdens of research to benefit others, nor should they disproportionately avoid the burdens of research and only reap the benefits.

As it applies to pregnant people, the argument is that a blanket ban – whether *de facto* or explicit – is unjust since it denies them the ability to benefit from research. Although it is fair to be concerned about the particular harms that research might have on a person when they are pregnant, as Francoise Baylis has said “pregnant women get sick, and sick women get pregnant” (2010) indicating a clear need for important information about medical treatment during pregnancy that can be gained from research. Denying pregnant people the ability to benefit from the information research gives them about which medical interventions are safe and effective for them goes against the principle of justice (Baylis & Ballantyne, 2016, p. 5). Without adequate information about medical treatments during pregnancy, either pregnant people are not getting adequate treatment for their needs because they or their doctors have decided the risk is too great, or they are receiving treatment that has not adequately been researched, effectively placing all clinical settings as experimental (Lyerly et al., 2008, p. 7).

It is fair to say, then, that pregnancy exclusions mean that pregnant people are not getting equal benefits from research, and furthermore they are disproportionately being denied benefits from research compared to their non-pregnant peers. The argument from justice says that it is ethically required to include pregnant people in research in order to balance the

disproportionate lack of benefits they receive from their exclusion. Since we have multiple arguments against the blanket exclusion of pregnant participants and two strong arguments in favour of their active inclusion, it is important to also address how that inclusion might look.

1.7 Responsible Inclusion

We know now that women have historically been excluded from research and the push for their inclusion still lags for pregnant people. Since the inclusion of pregnant people in clinical research is a new practice, it requires new sets of guidelines that can deal with the differences in the bodies and needs of pregnant participants (Lyerly et al., 2008, p. 7). Lyerly and colleagues suggest that legislation needs to change, and funding needs to increase in order to achieve this goal of including pregnant people in Randomized Control Trials (RCTs) as well as allow for observational studies (Lyerly et al., 2008, p. 16).

Baylis and Halperin present two suggestions for the responsible inclusion of pregnant participants in medical research: staggering and embedding (Baylis & Halperin, 2012, p. 140). The staggered approach begins Phase I trials for pregnant participants at the same time as Phase III trials for other participants so that pregnant participants will not be exposed to substances that do not pass Phase I and II testing. The embedded approach would be to allow pregnant participants to join late Phase II or Phase III trial alongside other participants, skipping Phases I and II for pregnancy, but enhancing the monitoring of pregnant participants to ensure safety (Baylis & Halperin, 2012, p. 142). Furthermore, the recruitment of pregnant participants could be staggered as well to first test safety on later term pregnancies before earlier terms with an increased focus on pregnancy-specific needs in the research process (Baylis & Halperin, 2012, pp. 142-3). Both the staggered and embedded approaches allow for added protections of the

fetuses that match their needs as vulnerable groups without completely excluding pregnant people from research.

Ells and Lyster suggest the use of ad hoc advisors to help answer difficult scientific questions about trial design for pregnant participants since there lacks empirical evidence for baselines or standards of care (Ells & Lyster, 2016, p. 105). These concerns and advice will be less prevalent in lifestyle interventions with minimal risk to parent and fetus (Mathews, 2016, p. 16). What this means is that each approach might have its own pros and cons that could make them more useful for some types of research than others and there is no one best way to include pregnant people. Chapter 4 will discuss general principles involving pregnant people in research and Chapter 5 will provide more guidance about specific policy like this and when it should be used.

Chervenak and McCullough (2011) suggest that we separate ethical criteria for research involving pregnancy into four categories: Phase I and II clinical trials aimed towards parental health outcomes, RCTs aimed towards parental health outcomes, Phase I and II clinical trials aimed towards fetal health outcomes, and RCTs aimed towards fetal outcomes (pp. 44-46). Each category has a set of risks that would be deemed appropriate for the study such as ensuring that parent-regarding research has no documented fatality and rare documented injury to fetuses, and for fetus-regarding trials that the injury and disease risk to the parent is low or manageable (Chervenak and McCullough, 2011, pp. 45-46). These are ways to ensure that research does not place all the burdens on the fetus or pregnant parent for only potential benefit to the other.

It is not enough to just insist that pregnant people are included in research as it currently

happens. Guidelines, policies, laws, and procedures that were created without them in mind might pose a barrier to the fair and safe inclusion of pregnant people in research. For example, there is currently no standard way of dealing with the issue of consent for a fetus' participation in research. Are they a participant at all? If not, what kind of protections can they be awarded? As many have suggested, moving away from simply labelling pregnant people as "vulnerable" can help alleviate concerns that a pregnant person's consent to research is somehow coerced or manipulated, but without clear guidelines on how to conduct ethical research on pregnant people that also passes scientific rigor, researchers and REBs alike will be hesitant to engage in this work.

1.8 Patient Perspectives and Current Needs

An important element to the discourse of the inclusion of pregnant people in medical research is participant perspectives (Jaffe et al., 2020, p. 6922). As expected, a main concern of pregnant people is the risk of harm to their fetus, rather than themselves, although, in one study, most indicated in response to hypothetical scenarios that this risk is not large enough to avoid many studies testing newly developed vaccines (Jaffe et al., 2020, p. 6923). For more innocuous interventions such as the use of over-the-counter probiotics in pregnancy, this calculation that the study is worth the risk seemed to increase when the pregnant participant considered being offered the experimental intervention, but also possibly decreased when one considered the possibility of receiving the placebo instead (Ballantyne et al., 2017, p. 480).

This hesitancy to participate in clinical trials because of the potential to be randomized into the placebo arm is an interesting factor. In fact, some potential participants of the probiotics in pregnancy study requested information about the probiotic in order to buy it,

making them ineligible to participate (Ballantyne et al., 2017, p. 482). This is an important aspect to keep in mind for two main reasons. 1) it goes counter to the expected concerns about taking ‘experimental’ treatments; and 2) it points to another downside of a lack of research that is not fully being considered. There is almost a feedback loop where pregnant people are recognizing that certain interventions are prescribed or recommended for pregnant people without clear research and have been provided to them for so long that the more likely scenario of harm comes not from taking the intervention, but from taking nothing. One problem with a lack of research is that it can create harms by reducing the chances of pregnant people taking medications when needed, and it is clear from these real-world examples that these harms are known by the general public, contributing to lack of interest in participating in studies that require placebo controls.

Wild and Biller-Andorno most clearly state the issue at hand “[f]or the discussion of how to include pregnant women in clinical research, and especially how to assess possible risks, clarity on who is the research participant is crucial” (2016, p. 130). Van der Zande and colleagues also emphasize the issue of needing to clarify “the moral status of the fetus” and whether they can be considered a distinct participant, or of joint interest with the pregnant parent (2016, p. 75). Lyerly et al. (2008) point to the complexity of having two separate beings, who could be considered two people, with intertwined health outcomes potentially have conflicting interests (pp. 17-18). Despite claiming that this is an important issue for moving forward with research involving pregnant people, none of these authors has clearly given an answer.

As a first step forward, Wild & Biller-Andorno do suggest a double unit model that

considers interests of pregnant parent and fetus jointly (2016, p. 132) to reflect the sense of joint being with the fetus that some mothers in their study expressed (Wild & Biller-Andorno, 2016, p. 126), and to avoid the harmful dichotomy that often pits pregnant parents against their own child (Wild & Biller-Andorno, 2016, p. 131). However, when examining Wild's explanation of the model, it relies on a "decisional capacity" account of personhood to determine the role of a participant (Wild, 2012, p. 90), which we will see in Chapter 2 is not a reliable way of understanding this concept. Chervenak and McCullough make suggestions to implement their "fetus as a patient" model in the research context (2011, p. 41), but despite having useful implications, using a model that was designed for clinical practice again cannot capture what it means to be a participant in clinical research. These questions must be answered so we can move forward with the responsible inclusion of pregnant people in research and rectify the injustice that has been committed through their continued exclusion.

Conclusion

There are two main reasons for the historical and current exclusion of pregnant people from medical research that can be categorized in the following ways: Reason 1) is the need or desire for "clean data" where anything that was seen as a difference, such as uteruses, were said to complicate a researcher's ability to efficiently determine results of a study for the general population, which incidentally excluded pregnant people. It later moved to directly exclude pregnant people when non-pregnant women and people who are AFAB were accepted into research. It has become more commonplace to desire representative samples in research, but the exclusion of pregnant people specifically remains either as an issue of logistics, or an issue of safety concerns, which brings us to reason 2.

Reason 2) is the worry that the pregnant person or their fetus is vulnerable to the harms of research more so than a non-pregnant person. Again, this historically took the form of excluding anyone who could become pregnant, sometimes even if this possibility was very low. Currently, the concern comes mostly from REBs who might be hesitant to approve studies involving pregnant participants if there is no clear indication of safety already.

Reason 2) can be split into three main motivations or implications for seeing pregnant people and their fetuses as vulnerable. 2a) a concern that pregnant people could be harmed or exploited by researchers; 2b) a concern that the competing interests of a pregnant person and their fetus is unresolvable and 2c) lingering misogynistic perceptions that pregnant people are irrational or incapable of making risk-assessment decisions for their own fetuses without external protection. These three motivations indicate that the grouping of pregnant people in the category of “vulnerable” must come with more detailed examination of what it means to be vulnerable and how different groups could be vulnerable in different ways so that vulnerability to exploitation, and vulnerability due to diminished capacity to consent are not conflated with vulnerability due to complex bodily changes.

Finally, underlining a lot of the discussion of “vulnerable groups” is also the implicit assumption that the fetus themselves are the vulnerable group, not necessarily the pregnant person, but since the pregnant person is the reason that the fetus is even involved in research, they must also be treated as vulnerable. After opening up some of these concerns for vulnerability of fetuses, the current debate has set up the question of *can fetuses be participants?* without ever answering it, pointing to the need for my work to fill in this gap.

Chapter 2 will address the conceptual view of what it means to be a subject or a participant of research and look at different ways in which fetuses and pregnant people can be involved in both clinical and non-clinical settings, with a focus on clinical outcomes. What this means is that the question of whether fetuses are participants and what that means for pregnant people in research is less clear in the clinical side of research, but drawing from non-clinical examples can help address some of the nuances that might appear. By doing so, Chapter 2 sets up the ability for analysis in Chapter 3 of four example cases. In each of these cases I will look at what role and involvement the fetus has and determine if they fit the conceptual role of a subject or participant that we will establish in Chapter 2. Chapters 4 and 5 then go on to answer questions about principles of consent, and specific policy changes for the TCPS2 that should arise to account for the status of the fetus before Chapter 6 addresses potential objections and perceived implications of this status.

Chapter 2- Focusing Our Vision

“Names matter because concrete individuals lie behind them”²

Introduction

Overall, my project aims to answer the questions of *can fetuses be considered participants?* and if so, *what are principles and guidelines for their inclusion in research?* So far, I have concluded that pregnant people should be included in clinical research in order to benefit themselves and their fetuses, and to align with the principles of autonomy and justice. The next step is to answer the question of what it means to be a participant in general cases, so that we can properly determine if a fetus fits this concept. When it comes to the role of participant for the pregnant person and their fetus in research, a few possibilities have been explored in the past including: “the fetus as a patient” (Chervenak & McCullough, 2011, p. 41), the fetus and pregnant parent are two parts of a type of joint participant (Wild & Biller-Andorno, 2016, p. 132; Lyerly et al., 2008, pp. 17-18), and the fetus is not a participant, but creates a complexity for the pregnant parent (Ells & Lyster, p. 108; Johnson, 2016, p. 174). Unfortunately, these proposed ideas are not strongly defended or developed, but rather given as brief suggestions for others to flesh out and apply.

Chervenak and McCullough (2011) do present a strong case for the consideration of fetus as a patient in medical practice and apply this to some research contexts, but the application it has to answer the questions of what it means to be a subject or participant in research is limited

² Bibace, R., Clegg, J. W., & Valsiner, J. (2009). What Is in a Name? Understanding the Implications of Participant Terminology. *Integrative Psychological & Behavioral Science*, 43(1), 67–77.

since, as they say in another work, its definition includes an expectation for “clinical interventions that are reliably expected to protect and promote the interests of [the fetus]” (McCullough & Chervenak, 1994, p. 104). Although fetal research often involves stringent protection for fetal interests, we will see from the coming sections that this is not a sufficient conception for the general role of a subject or participant in research.

When it comes to determining who counts as a participant, there is currently no clear answer. Firstly, it is not even clear what it means to be a participant and why this might be different from other terms like “subject” or “collaborator.” As evidenced by important research ethics documents such as the Belmont Report, first published in 1979, humans were previously considered “subjects” of research, which was the same term used for non-human animals and cadavers. This term lost its popularity over the next few decades for two main reasons: a linguistic preference for the involved term “participant” by publication guidelines and a practical shift in the research process that actually included the desired involvement. Beyond “participant” there has also been a shift towards term such as “partner” and “collaborator” when the participant becomes involved in the formation of the research question and study rather than just participating in its execution.

This chapter will examine different ways in which a being can be affected by or involved in research and how these might be labelled. For example, an adult filling out a survey might be considered a participant of research, but a dog being introduced to a mirror might be considered a subject. The conclusions of the chapter will carve out a general separation of who does and does not count as a subject, participant, or other involved being. For example, a parent who drives their child to a research lab might be affect by research and involved in the research

process, but they are unlikely to be considered a subject or participant since their data is not analyzed for research outcomes. The purpose of this chapter is to establish foundations on which to examine the case of pregnant people and their fetuses in Chapter 3 in order to determine in which cases a fetus could be considered a subject, a participant, both, neither, or something else. Chapters 4 and 5 will then go on to discuss the principles and guidelines that should come with the status of the fetus and how we need to consider the relationship the fetus has to the pregnant part as part of our analysis.

To determine the various ways of being affected by research, this chapter has seven sections. 2.1 presents the problem as it currently stands when it comes to defining participant, subject, or other terms. Sections 2.2 and 2.3 look at descriptive and prescriptive accounts of the terms “subject” and “participant” respectively to examine both the linguistic preference for the term “participant” and the different ways in which one can be involved in research. 2.4 briefly touches on other terms such as “partner” and “collaborator” and how they fit into the discussion of participation. Section 2.5 then lays out three types of data analysis in research that determines one’s level of involvement in the research, including what it means to be non-involved. Section 2.6 summarizes the differing types and distinguishes the conceptual terms “subject” and “participant”—namely that “participant” will be reserved for research where the human or animal has intentional involvement, leaving some humans as subjects in certain research and opening up potential to include some animals as participants. Finally, 2.7 provides clarity about participant status for children but not fetuses. The status of the fetus will be examined in Chapter 3.

2.1 The Problem

It has become more commonplace recently to use the term “participant” in reference to humans involved in research, rather than the more outdated term “subject.” “Subject” is still commonly seen in non-human animal research so some might intuit that the descriptive difference between a subject and a participant in research is the line between non-human and human. The idea here would be that animals who are subjects of research, like mice, hamsters, or dogs, are not capable of consenting to the research being performed and, therefore, the regulations and guidelines around their involvement do not include a consent process. On this view, humans are participants because they are capable of consenting to research and their consent is required for their participation. In essence: non-human animals are subjected to research, but humans voluntarily participate in it, and the shift to ‘participant’ is meant to capture the importance of this distinction.

The problem with this separation between subject and participant is that it cannot account for many common cases that we see in both clinical and non-clinical research settings. First, labelling all non-humans as incapable of consenting in a strict sense is probably correct, but labelling all humans as capable of consenting is not. Most young children up to about age 9, and many children up to about age 11 do not possess the cognitive capacities to understand research (Hein et al., 2015, p. 2). For this reason, many children are not considered capable of providing formal consent for their own involvement, but they can still be involved in the research (Canadian Institutes of Health Research, 2022, p. 40). There are also many conditions that could interfere with an adults’ capacity to consent such as dementia, fragile X syndrome, or a comatose state. In these cases, people do not have the capacity to consent but are required

to have a designated guardian who can provide proxy consent for their participation.

For the purposes of this project, I will be using the term “consent” in a very specific manner. Consent is the specific legal and formal process of agreeing to research participation. What that means, is that even if the potential participant has provided every reasonable step to assure the researcher that they are aware of the research project, their rights, and the risks, if they have not met the legal and guideline requirements for consent for that particular type of research (often a written consent form signed by an adult) they cannot be said to have provided consent. Another scenario to find in research, however, is someone who is intentionally involved, but consent was not required for their involvement, such as with the Twitter case that we will discuss in more detail later.

The term “intentional involvement” is meant to cover cases of involvement that do not always meet legal specifications of consent, but still include clear intention. On the other hand, some people are not capable of being intentionally involved in research, but they would technically meet the level of legal consent if there were a proxy who provides legal consent on their behalf based on the formal process and requirements. Therefore, there are possible cases of intentional involvement without consent, and probably many more cases of legally obtained consent without intentional involvement of the researchee themselves. By focusing on the concept of intentional involvement, I am exclusively looking at cases where the being involved in the research has become involved knowingly and intentionally, regardless of whether they meet legal concepts of consent, and excluding cases of people – such as older children – whose legal proxy consent has been obtained despite their personal intention in the research.

The concept of proxy consent was introduced in 1964 in the Declaration of Helsinki as a

way to ensure ethical conduct in research for all humans regardless of their ability to consent themselves (Varadan et al., 2021, p. 288). The role of the proxy is to act on behalf of the individual and provide voluntary, informed consent if they find that the research is in the best interests of the potential participant. However, the details of the proxy's role are not clearly elaborated on in the Declaration and other guidelines, often pushing the onus of determining a good proxy onto local legal standards (Varadan et al., 2021, p. 289).

As it pertains to children, the International Council for Harmonization (ICH) requires that adults providing proxy consent for children in research must be a legally authorized representative of the child and must be "legally competent and capable of providing informed consent" (Varadan et al., 2021, p. 290). In addition to this, the UN Convention on the Rights of the Child (CRC) adopted in 1989 frames the role of the proxy in the consent process as that of an advocate for the rights and wishes of the child, rather than as an entitlement to the decision-making over the child, recognizing that a child's capacity to understand the consent process will evolve over time and it is the guardian's responsibility to support and guide these capacities (Varadan et al., 2021, pp. 295-6).

For adults, the aim of the proxy decision maker, otherwise known as a substitute decision maker (SDM), is a little different since adults have had more of a chance to express wishes about research either before they are ill enough to need a proxy, or presently during the process. In addition to acting as an advocate for the rights and wishes of the individual, a proxy for an adult must also try to make a "value-congruent decision" to support the autonomy and ensure that the consent given is voluntary and informed (Shepherd, 2022, p. 5). This includes ensuring that one is properly informed about their role as a proxy, and not just informed about the

research in question (Shepherd, 2022, p. 4). The role and process of proxy decision-making can be complicated and unclear, but overall, the practice is that of an advocate, likely a guardian, providing consent to participate in research for their dependent, whether that is a child or an adult. The proxy is not the one involved in the research outcomes, but a stand-in for the person who cannot consent for themselves. It is important to note that the role of a proxy is not about having the right to provide consent on behalf of someone in your care, but rather the responsibility of providing or refraining from providing that consent in their best interest, in line with what they would want, and with their current capabilities in mind.

There are also cases where autonomous humans are not required to consent to research because of the type of research conducted and the jurisdiction in which it takes place. This is usually the case in non-clinical settings, but the examples can illustrate the boundaries of involvement and consent for clinical research as well. One example of research not requiring consent is the use of posts (tweets) from the social media site X (Twitter). Research using Twitter data, such as tweets and short biographies, is often conducted without the consent, or even knowledge, of the tweet authors in part because the terms of service of the site provide X the company with rights over the information posted including providing permission to use for research, and partly because the tweets are publicly accessible information and therefore do not require consent from the tweet authors to be used in research (Fiesler & Proferes, 2018, p. 1).

In addition to the Twitter example, it is not required to gain consent for access to national data for research in Denmark (Thomseth et al., 2019, p. 508), which means that a lot of research is conducted through access to national records. In both of these cases, the autonomous adults

who are being researched are not required to consent to, or even be informed of, the research in which they are supposedly participating. Therefore, from a descriptive perspective, it is not as simple as associating the term “subject” with non-humans who cannot and do not consent, and the term “participant” with humans who can and do consent to research because sometimes humans who cannot consent are still required to have proxy consent and sometimes adults who can consent are not required to provide any.

Notably, guidelines such as the one put forth by the Council for International Organizations of Medical Sciences (CIOMS) specifically use “subject” and “participant” interchangeably (CIOMS, 2016, p. xii), and the Canadian Tri-Council Policy Statement (TCPS2) prefer “participant” for all research contexts, (Canadian Institutes of Health Research, 2022, p. 15), thus removing any consistency in how the terms are commonly used in research. In the sections that follow, I will examine different types of clinical and non-clinical research and how the role of the researchee, whether they can be called a subject or participant, affects the level of consent, assent, or mere lack of dissent, required for their involvement. By doing so, we can determine how Western bioethics in general and Canadian bioethics in particular currently define the role of the participant and use this case to apply to fetuses in order to answer the question of whether fetuses can be participants in clinical research.

Weaker than consent, assent is “a prospective indication by an individual of her willingness to participate in research” (Kantian & Wendler, 2015, p. 461). This does not require that the human or non-human animal in question is fully informed about or capable of understanding the research, but still involves securing some form of agreement to participate in the activity that is being performed for research purposes. In contrast to this, dissent is “an

expressed objection, either verbal or behavioral, to what an individual is experiencing as a result of a research procedure” (Kantian & Wendler, 2015, p. 461). Sometimes in research contexts it is not possible to ascertain consent or assent from the researchee, but acts of dissent are clearer to determine. Whether a researchee will be asked for consent, assent, or whether researchers will be merely looking for a lack of dissent depends on the developmental capabilities of the being in question (Brothers et al., 2020, pp. 130-131) and which method is best suited to protect the interests of the being (Kantian & Wendler, 2015, p. 470).

2.2 Subject: Descriptive and Prescriptive Accounts

The term “subject” used to be more widely used for human research. Etymologically, it has a root association with the Latin terms *subicere* and *jacere*, which mean to subject to conditions, and to throw, respectively (Bibace et al., 2009, p. 68). The significance of this is the imagery of the subject of research is being mistreated, subjected to harsh conditions, or thrown around based on the desires of the researcher. This association of instrumentalization of the subject begins centuries ago where research was mostly performed through dissection on cadavers and only later, in the early 19th century, began to refer to live humans (Bibace et al., 2009, p. 69).

It is likely no surprise that associating research on live humans with that of cadaver dissection or animal testing is seen as undesirable. It is not uncommon to hear a negative attitude towards the comparison of humans and non-humans, and use of the term “guinea pig” as a pejorative for “research subject.” There is a sense that, to be treated as an animal subject in research is to be treated poorly. To some degree this attitude is very much warranted. Research involving non-human animals is often in the form of “animal testing” for product safety, placing many of them in harm’s way in order to have data about human consumption

with no benefit to the animals themselves.

It is important to note here, however, that many animal subjects in research are still governed by ethics guidelines. The International Council for Laboratory Animal Science (ICLAS) has guidelines for research that outlines “the three Rs” of research with laboratory animals: reduction, replacement, and refinement, which seek to reduce the number of animals used in research and the harms that are brought against them (Kantin & Wendler, 2015, p. 459). Many do argue that these guidelines are not enough to protect animals from harm in research scenarios and advocate for the end of all animal experimentation aimed at human benefit.

It is also the case that research on non-human animals is not just done for the benefit of humans but is also done to study research questions related to animal health. In the United States, this research would be covered in part by the Animal Welfare Act (AWA). This type of research involving animals can be far more ethically justifiable and does not always fit the “guinea pig” image in the same way as experimentation for human benefit does. Therefore, despite the negative associations with the terms “subject” and “guinea pig,” to be a non-human research subject does not mean that one is necessarily treated without any regard for their welfare. For the purposes of my future arguments, I will be referring to research involving non-human animals to mainly include research for the purposes of benefitting of non-human animals and not more typically imagined research for the benefit of humans.

Still, despite the protections for animals and recognition that they might have some agency-based abilities, there is no current guideline recommendation to involve a consent process by proxy, or direct assent or dissent from the animal to ensure the individual’s

willingness to participate (Kantian & Wendler., 2015, p. 459). Although authors such as Andrew Fenton have been advocating for this addition (Fenton, 2014, p. 130). There is still room for improvement when it comes to protection and respect of non-human research subjects. However, just as with non-human research, this does not mean that being a human “subject” of research indicates a level of disregard for one’s safety since we have seen that it is still an acceptable term for use in human research according to many international guidelines which take human dignity and respect very seriously.

There is, however, an inconsistency in how these terms are used. Since some guidelines and authors indicate a desire to use the term “participant” for particular purposes, as we will see in section 2.3, it seems like those who do not fit the purposes of “participant” should continue to be called “subjects,” even though that is not the case with current guidelines. For example, since the term “subject” produces imagery of being subjected to certain conditions, one might be inclined to call someone a research subject when they have little control over the research conditions beyond consenting to take part and reserve the term “participant” for those who are more actively involved. As we will examine further in section 2.5, being involved in research is not just about autonomy or consent and we cannot attribute terms like “subject” or “participant” to a being based solely on their level of autonomy. Involvement comes in different forms that also depend on the type of research being conducted.

2.3 Participant: Descriptive and Prescriptive Accounts

More recently in Western research involving humans, there became a preference for the term “participant” over that of “subject.” There are two overlapping reasons for this change. The first is a linguistic preference for a more palatable term that denotes respect towards the humans

involved in the research, and the second is a change in the actual involvement and care for these participants. As Bibace and colleagues put it, “names matter because concrete individuals lie behind them” (Bibace et al., 2009, p. 76), indicating that the need for a more respectful term would have its own practical benefits, even if the role that participants played in comparison to subjects did not change. The practical benefits would come in the form of increased trust or a better experience for the research participant when they are shown a certain level of respect.

Subjects are often seen as instrumental pieces to advance the knowledge gain needed for the research but are not themselves the beneficiaries of the knowledge (Biruk & Prince, 2008, p. 240), making the shift towards “participant” one of a shift in the goal of research. Researchers are no longer gaining knowledge for the sake of knowledge, but rather looking to benefit the community participating in the research, and perhaps in turn benefiting the individual participant directly, although direct benefit to the participant is not the main goal of research. The role of the participant is more complex and nuanced than that of the subject and could include roles of advocacy, collaboration, advisory, and analysis (Bromley et al., 2015, pp. 905-6).

In Chapter 1, we discussed this concept of benefits by looking at the how participants can be compensated for their participation in research, and how research questions that aim to improve the health and lives of the types of participants involved could in turn benefit the participants later on. This is the main reason why McCullough and Chervenak’s (1994) “fetus as a patient” concept does not apply well to the question of fetuses as participants, since it relies on a concept of medical practice and therapeutic benefit that we do not always see in the research context. If you will recall, unlike treatment, the goal of research is not to benefit the

participant directly, but this does not mean that the researchers are free from looking to provide benefit where possible. With unethical and exploitative studies that occurred in the past such as the Tuskegee syphilis study and the experiments forced on captors in Nazi concentration camps, these benefits did not occur, increasing the association between subject and instrumentalization. But when one is provided with opportunities to benefit from the research in which they are participating, such as potential having their community needs addressed, the feeling of instrumentalization could decrease.

The important element here for Biruk and Prince that indicates a change in how one can be involved in research is the shift from being subjected to research for a goal decided by the researcher as a need, to participating in research with a goal to improve the health and wellbeing of the community in which you live, or the lives of people similar to you (Biruk & Prince, 2008, p. 241). It is unfortunately common that researchers benefit greatly when picking particular research questions because it provides them with funding or career opportunities, but the community that they choose to study does not see the same benefits from the outcomes of this research (Walcott, 2020, p. 1). When those asked to participate in this research do not see their needs reflected in the research question or how they are treated through other benefits offered to them, they could feel disrespected or instrumentalized, especially if this occurs often for their community.

It would seem that the distinction between a subject and a participant could be the goal of the research and whether it is designed to benefit or exploit the people or community being researched. Since we began using the term “participant” around the same time we began ensuring that research did not exploit those involved, then beneficial research goals involve

“participants.” No one wants to be the “subject” of an unethical or illegal experiment that is solely meant to improve the lives of the researchers or what they see as important. Thankfully, ethics guidelines and legal regulations have drastically reduced the chances of exploitative research occurring, and it is especially unlikely for a study to be approved by a research ethics board if the research has no purpose and those involved are subjected to unfavorable conditions.

What this highlights, then, is that participants have more agency over their involvement in the research than subjects do. Through the process of consenting for themselves, or through other means of intentional involvement, the participant exercises this agency of whether they wish to be involved. A subject, although still part of an ethical research project, does not have this same control. As we will see in section 2.5, they are either a subject due to the research using their publicly available or previously stored data, or they are a subject because someone has justifiably consented or agreed on their behalf when they were unable to consent for themselves. The distinction between a participant and subject is not one of ethical or beneficial studies, but related to this concept of intentional involvement that comes from this agency.

Although Biruk and Prince can help us point to a shift in ethical obligations of researchers and research questions, we should not take their arguments to mean that ethics guidelines that currently use or allow the term “subject” are in any way less ethical than ones that use the term “participant.” However, what we can take from their arguments is that some research seems to involve the researchee in more ways than others. As we will see in section 2.4 with terms like “partner” and “collaborator,” there are research methodologies that are designed to involve non-researchers at levels beyond data analysis. So perhaps the important distinction between a

subject and a participant is not about respect or exploitation, but rather just about their level of involvement and whether the “participant” in question is actively involved in the research in a way that the “subject” is not.

In a similar vein to that of respect, it might be tempting to align the term “participant” with that of “person” in the concept of personhood, but this would also be a mistake. Personhood is a moral concept that categorizes which beings have a certain moral consideration that needs to be respected. Most commonly, personhood focuses in on concepts such as rationality and autonomy. These describe a being’s ability to have desires and make deliberate or reflective decisions about their own enjoyment, interest, and quality of life (Gruen, 2021). The idea is that beings who have personhood or this ability to make decisions about themselves deserve a higher moral consideration for their life or wellbeing than beings who do not possess personhood, which might suggest that only persons can be participants while non-persons are subjects.

This again could lead us to conclude that all participants have agency and require consent to participant in research since an important aspect of personhood as it pertains to research ethics is a respect for autonomy and seeking out one’s ability to consent (Canadian Institutes of Health Research, 2022, p. 6). The Belmont Report, which uses the term “subjects,” focuses on “respect for persons,” while acknowledging autonomy and protecting those with diminished autonomy (D’Angelo, 2019, p. 58). However, despite using the term “persons,” the implication here is that one does not need to be autonomous to be a person deserving of respect in research. Even though the Belmont Report uses the term “persons” their claim is about humans, not the moral concept of persons as it pertains to personhood. This is significant because it shows that

the guidelines are not meant to be protection for persons who have personhood in the sense of autonomous rational agency, but rather protection for all those involved in research. Since the report is for human research, it does not cover non-human animals, but it also does not exclude any human that might be considered a non-person due to a lack of autonomy. It is, therefore, an unsatisfactory answer to suggest that participant status is dependent on moral personhood since there is clear separation between the decision to use the term “participants” and persons.

Now that we have seen how “subject” has been used, and why “participant” is often preferred, let’s take a look at some recent uses of the term “participant” in research. The Canadian TCPS2 uses “participant” to refer to all research involving humans in order to convey respect and capture varied degrees of involvement (Canadian Institutes of Health Research, 2022, p. 15). Importantly, the American Psychological Association (APA) publication guide prefers the term “participant” but recognizes that the term is dependent on the methods in the research and leaves the final decision up to the researcher (Bibace et al., 2009, p. 74), suggesting that a large use of the term is based on this linguistic preference to show respect and a style preference for publication of research findings.

Looking at the descriptive uses of the term “participant” we can see that its usage reflects the desire to show respect for humans, but not necessarily to provide more community-desired research projects since the TCPS2 uses the term in all scenarios regardless of what type of research takes place, and there is a style preference for the term in publication. This indicates that the current difference between the usage of the two terms “subject” and “participant” is not indicative of a difference in the type of research taking place. The indication here, then, is that respecting the humans who are involved in research, regardless of how that research is

conducted, is quite important to some policy makers. However, it can still be important to keep in mind that there have been stated prescriptive goals of moving towards the use of the term “participant” that might inform how it is used in the future. For clarity, I will be using the conceptual terms “subject” and “participant” quite distinctly to indicate a difference in the level of involvement a being has in research in Chapters 3 & 4. This distinction will be explained further in section 2.6. In Chapter 5, and within the context of the TCPS2, I will be using the term “participant” to refer to both conceptual subjects and participants since that is how the term is used within the guidelines.

2.4 Partner, Collaborator, Co-Researcher

Beyond the shift from subject to participant, there is a rising trend with terms such as “partner,” “collaborator,” and “co-researcher” that was more clearly made with a practical shift of involvement in mind. Community-based participatory research (CBPR) is one such way in which involvement in research goes beyond participation in its execution. CBPR is a practice that sees community and researchers as “equitable partners” (Jacquez et al., 2013, p. 176) and shift the power dynamics that place researchers above their participants (Biruk & Prince, 2008, p. 237). Participants in this research might be called “partners” or “collaborators” because of their involvement in the shaping of the research goals, the methodology of the research, and the dissemination of results (Bodén, 2021, p. 8).

The involvement that CBPR provides is preferred by many marginalized communities who experience a level of research fatigue when they participate in research that is not aimed at achieving any goals they see as priorities. Research fatigue can also come from marginalized communities being over-researched due to their needs posing interesting or important

questions for researchers. However, this fatigue can be exacerbated by the feeling that research questions come from an outside view of what the community needs and do not have actual goals or interests of the community in mind, which is why CBPR can help lessen some of this feeling of fatigue.

Community-based organizations and their members have been shown to take an interest in participating in research when the research goals match their community goals and when they do not feel that participating is simply a way to be used as a means to further the needs of the researcher (Biruk & Prince, 2008, pp. 240-1). To illustrate this, take a moment to consider three different research studies involving humans: the first is a stress test performed in a lab where healthy people of a wide range of abilities undergo a series of physical exercises while attached to probes that monitor things like vital signs, perspiration, and muscle tension. The goal of this research is simply to improve medical kinaesthetic knowledge; not to test any medical intervention or treat any medical condition. In this case, one might feel very instrumentalized by participating in the research because they are subjected to stress conditions and there is no clear benefit to the outcomes of the research from the perspective of the participant.

The second study is one where a new allergy medication is being tested in a Phase I trial. Recall from the introduction that Phase I trials are done to test the safety in humans of medications that have previously been shown to be safe in non-human research or to test dosing. They are not ones that test efficacy or effectiveness of the intervention in question. What this means in this case is that people without allergy symptoms are recruited to participate in the study and receive small doses of the new medication or some of its components to see

what kind of side effects might occur. They are not being recruited to test if the medication is effective at treating allergies. In this case, the people might feel like they are contributing to a benefit for the community because, although they are not benefiting from taking the medication, they can see a need for it to be produced and a benefit for others if the research proves successful.

The final study is a Phase III trial of the same allergy medication. Phase III studies test the optimal dose of the intervention against a standard of care, or a placebo. What this means is that people who suffer allergy symptoms participate in the research that has the goal of gaining knowledge about how the new medication performs in comparison to current medications on the market. This is a general benefit of research for people who are allergy sufferers. There is also a potential for those in the study to directly benefit from their participation if the medication is superior to what they have previously taken but recall that the goal of research is not to benefit the participant and these benefits are not guaranteed. Even just considering the benefit to allergy sufferers in general, it is fair to say here that these people are less likely to feel instrumentalized than those in the first example who were performing physical labour and were unable to see the purpose.

A study using the CBPR method would start with a community member or organization expressing a desire for a new allergy medication. They would then be involved in other aspects of the study like recruitment of healthy members for the Phase I trial, or allergy sufferers for Phase III. Those who are involved in the research would not simply become part of it during recruitment and after all the other steps were performed by researchers alone. The CBPR method reduces feelings of instrumentalization and holds a level of involvement beyond that

of what we have seen for subjects and participants, which is why terms like co-researcher or partner have developed.

Like we have seen with the difference between “subject” and “participant,” what makes someone a partner or collaborator is less about the research goals and more about the role that the individual plays. Although CBPR is a particular study design, there are various ways of involving researchees beyond this method that could land them in the role of research collaborator. What separates a collaborator from a typical participant is that they are intentionally involved in aspects like research design and knowledge dissemination.

The distinction between subject and participant can also be explained through the examination of the involvement of the role. A “subject” of research appears to be one who is not intentionally involved, whether this be due to their inability for intentional involvement, like a non-human animal, or their role in the study that does not require their intentional involvement, which we examine further in section 2.5. Participants are those who are intentionally involved in research through providing their data for analysis of research outcomes, but not ones who are involved in other parts of research like a partner or collaborator might. In section 2.5 I will be looking at three ways to be involved in research based on the type of data analysis that is taking place and use these two separate subjects from participants in general cases of both clinical and non-clinical research.

2.5 Three Ways to be Involved in Research

As we have seen with all the terms examined here, there are different ways to be involved in the execution of research in such a way that one’s involvement is limited by research guidelines. There are a few different factors that determine the type of involvement one faces

and the principles and guidelines that are then put into place for their protection. One's level of involvement can first be assessed by their data analysis type. I have chosen to separate this into three types, the third being "non-involvement," so it is fair to think of it as two types of data analysis and a third, lack of analysis. Each type of analysis can be performed knowingly or unknowingly on the person involved depending on the circumstances. These three types only look at what could be considered a subject or participant of research, since they do not address involvement beyond the execution of research such as collaborating on the research question or recruitment.

Type 1 is when one's product or data that was generated outside of the current research conditions can be studied or analyzed for the purposes of the research question. Type 2 is the broad range of research that can occur in clinical and non-clinical settings. For example, in non-clinical settings, one provides data for analysis, such as survey answers about demographic or income information, health and wellness, and in clinical settings, one undertakes an intervention and provides data ranging from answering survey questions about the intervention to tissue samples for analysis. Type 3 is when a "non-involved" person provides support for the involved person that might resemble involvement but is distinct from it.

Type 1 can include things like the Twitter example where one produces tweets for an independent purpose that are then analyzed for research. However, it can also include secondary analysis of data that was produced for a previous research study. For example, if someone agrees to provide a blood sample for a study about diabetes, the researchers might store the unused portion of the blood and other researchers might analyze it later for a study

about blood types. Ethical guidelines dictate that secondary use can only be performed if the person previously consented to their data being used in further studies, but due to anonymization, it is rare that they are informed when the second study takes place. In other words, when the blood was drawn for the diabetes' study, the researchers would need to clearly and specifically ask if they are allowed to store the blood to be used for other research purposes, but the researchers who access the blood later on would not be able to figure out whose blood it was and contact the person about the new study. This means that one might regard them as having provided consent for the research, but not to be intentionally involved in this particular study.

In both the Twitter example and the secondary analysis blood type example, the data being analyzed were not explicitly produced for the current study, and in some cases, like with most Twitter studies, the people who produce the data are not even aware the study is taking place. It is also possible, however, that a researcher decides to notify Twitter users about their study and provide them the opportunity to opt-out. Perhaps the researcher makes an announcement using a popular hashtag so a large number of Twitter users who search the hashtag will see the tweet. The researcher plans to collect data about people who use the same hashtag and has told them that if they do not wish their data to be analyzed, to use a second hashtag at the end of each tweet.

Since the researcher is not required to obtain consent, it is not vital that all Twitter users see this tweet or know about the study and it is not reasonable to assume all people who do not use the second hashtag are actually agreeing to participate, but it is possible to imagine that a few Twitter users are happy about the study and they reach out to the researcher to give explicit

permission to use their tweets in their research. Since there is no formal consent process, these Twitter users still have not consented to the research, but they have intentionally involved themselves in the study.

For data analysis type 1, those unaware of the studies are subjects, not participants. This is because they do not fit the description of intentional participation in the study, regardless of their capacity for consent. So autonomous adults as well as non-human animals, young children, and those with relevant cognitive disabilities are always subjects because their data is being analyzed and subjected to the research, but they are not participating in it in any intentional sense due to their lack of knowledge or acceptance. Furthermore, in the Twitter case, even if some of the subjects were aware that their data was being used, if they have not provided it for the research purposes like the eager users who reach out to the researcher, they are not intentionally participating in the research and are still subjects. This is consistent with the separation of subject from participant and can allow us to capture what it means to be a partner or collaborator beyond being a participant by looking at the level of intentional involvement one has and whether that involvement include pre-produced data, new data, or study decision-making.

Data analysis type 2 includes all clinical and non-clinical research where the data is being produced specifically for the current research purposes. This would include a survey that one fills out about their health, and a diabetes study where blood samples are provided directly for the purposes of the study. It also includes any research where a researcher provides an “intervention” for the person in question. This could involve a medication to treat dry eyes, an exercise regimen to increase stamina, or a diagnostic tool for cancer. Again, this level of

involvement can be completed knowingly, such as when an adult willingly participates in a survey about their commute to work or takes a new medication to study its effects. It can also be completed unknowingly such as when a child's information is provided for analysis, or a child starts a new exercise regimen initiated by a parent who does not tell them about the research. The child is still involved in the research because it is their data that is being analyzed, and it is still type 2 because the data are being produced for the purposes of the study, rather than for something else, but the child is unaware of their involvement because of their age and their parent as an SDM has determined this to be an appropriate approach. This can also be true for adults with dementia or relevant cognitive disabilities that prevent them from being aware of their participation. There is still consent for their involvement through the SDM, but the fact that they are unaware means they are not intentionally involved themselves.

For data analysis type 2, the involvement in the research usually requires some level of knowledge about the study since the data would not have been produced if the study did not exist. Unlike type 1, it would not be possible for one to be knowingly but not intentionally involved in a type 2 study since the intention would come from actively producing the data to be analyzed. However, like type 1, there will still be instances where some people are not capable of being aware that it is their data that is being analyzed in research, so they are neither knowingly nor intentionally involved, placing them more in line with research subjects than intentional participants.

Finally, type 3 data analysis is better seen as "non-involvement," but it is still important to note. As we have seen with the differences between "subject," "participant," "collaborator," and other terms, the minimal type of involvement that one has in these cases is of types 1 or 2

because they are the ones producing the data under analysis. What this means is that in cases of type 2 where a guardian, advocate, or support person for non-human animals, young children, adults with certain cognitive disabilities, or even autonomous adults who simply request help from a friend, there might be actions that appear to be involvement in research. Let us explore this with the example of a young child. For the purposes of type 2 data analysis, the guardian who drives the child to the study centre, plays with the child under observation, or manages the child's at-home medication is not involved in the study unless the data collected for research analysis is produced by the guardian in some way. In this case, the guardian's data analysis is type 3.

Signing a consent form on behalf of the child, giving a phone number, or taking time to transport the child is not involvement in research, regardless of the mental load it places on the parent and their knowledge of the study, because their data is either not being collected or not being analyzed. Note here that, again, the relevant factor of making someone a subject or participant is not the signing of a consent form since the SDM, who signs the form and provides consent, is not the subject or the participant of the study when their data is not being analyzed. This is the common practice currently in research where children require proxy consent and it is not my intention to change that practice, despite calling this type 3 involvement. Only if the researchers require the guardian to fill out a survey about their *own* health or perform their *own* tasks that are monitored and recorded, regardless of the goal of the research project, the guardian can then be said to be involved as type 2 and might be a subject or participant. This will become important for analysis in Chapter 4 as we begin to look at which cases perhaps the pregnant parent may not be a subject of research in which the fetus is involved.

2.6 Subject, Participant, and Their Distinction Going Forward

Leaving aside the linguistic desire for a term that conveys respect, there is one key factor that underlines the difference between a subject and a participant: intentional involvement. This is separate from that of consent, since consent is a legal and formal process and for some young children, consent is required despite their inability to intentionally involve themselves in research. As we have seen, the term “subject” evokes imagery of being subjected to certain conditions. This can sound like an act of harm, but it more neutrally denotes the level of intentional involvement that the subject has with the research goals and intervention. Since guidelines still leave room for the term “subject” to be used respectfully, and there is an association with the term “participant” and the type of involvement that occurs within research, continuing to use the two terms interchangeably has the potential to both offend those who prefer “participant” as a sign of respect when “subject” is used, and confuse those who see “subject” as a more passive role when “participant” is used in passive research such as type 1. This latter point becomes important when we further examine a survey about Twitter research in the next few paragraphs.

Starting with the use of non-human animals, research will often *involve* the animal in physical ways such as attaching probes to measure brain activity, but the animal is not intentionally involving itself in the research since they are unaware of the research goals and they are, in fact, being subjected to these conditions. The protections laid out for non-human animals can help ensure that this subjection is not harmful and is done in the best interest of improving medical knowledge about non-human animals. Coupled with the common usage in human research guidelines, this protection for animals supports the continuing use of the term

“subject” in some contexts without it being a term of disrespect.

Although they use the term “participant” in their article, Fiesler and Proferes (2018) put it in quotation marks in the title, potentially acknowledging that calling Twitter users “participants” when they are unaware of the research is only a style choice and does not fit what one might normally associate with a research participant. They conducted a survey of Twitter users about their knowledge and opinions on research using tweets and biographies and discovered that nearly 65% of survey respondents said they believed permission should be required for this type of research. Furthermore, most would at least like to know that the research is being conducted (Fiesler & Proferes, 2018, pp. 6-9). Fiesler and Proferes attribute these opinions by Twitter users to a desire to be treated with some level respect, pointing out that asking for “permission,” as survey respondents indicated, is not the same as requiring full consent that other research might require. It is reasonable to assume that some people whose data ends up in research like a Twitter study would be upset to be called “participants” when they did not give permission since they did not actively participate in anything.

This leaves room for Twitter users to also be considered subjects when they are aware of the study but have not provided permission or consent for their data to be used, since it is not required of the researchers to gain this permission. If we return to the example of the Danish study, recall that in Denmark, consent is not required to access national data for the purposes of research. This means that the subjects (as they were called) of the study were likely unaware that their data was being used for this particular reason, and some were perhaps unaware that their data could be used at all. However, many Danish citizens could be aware of this rule and seek out information about the studies in which their data is used, giving them a level of

knowing involvement that others in the same study do not have. This is still not enough to make them participants.

So, there are two things happening here that makes these people subjects, not participants, of research. When type 1 research is conducted without the knowledge of those who produced the data, there is still a level of involvement that takes place, enough to call them subjects, but there is no intentional involvement by the subject themselves. However, if the study is type 1, and the subject is *knowingly* involved, but did not choose this involvement, they still cannot be said to be *intentionally* involved like a participant. If the goal of using the term “participant” is not only to convey respect, but to indicate a shift in the relationship between the researcher and the participant, then these cases do not meet that goal. One must be intentionally involved, like the eager Twitter user, to be a participant.

Since the protections for non-human animals and the common use of the term “subject” in international guidelines allows room for “subject” even when one’s dignity and wellbeing is thoroughly protected by guidelines, and since the term “participant” is associated with a particular type of research relationship, it would be beneficial here to reserve the term “participant” for the cases where intentional involvement takes place, and for Twitter users or Danish citizens who are unaware that their data is being analyzed for research, the criterion of intentional involvement is not met, making them research subjects. For one to be considered a participant, the researchers might still be the ones to place them under some conditions, which would meet the criteria of being “subjected to” research, but their awareness and *acceptance* of these conditions takes them out of the realm of subject and into that of participant.

In cases of type 2 involvement where the participant is actively choosing the intervention,

or in type 1 where they are aware of the research conditions and intentionally choosing to be subjected to them, they are no longer a subject, and are now a participant. Arguably, this excludes most non-human animals from being participants most of the time. However, it is possible for a non-human animal to be intentionally involved in research if they have the capacity for such involvement through the use of assent. Recall that assent is “a prospective indication by an individual of her willingness to participate in research” (Kantian & Wendler, 2015, p. 461), which is something that a chimpanzee might be capable of expressing in certain research contexts such as having probes placed on their body (Kantian & Wendler, 2015, 468).

The criteria for participation do not necessitate that all humans are always participants, since not all human subjects are even aware of their involvement in research, such as with the Twitter research, nor are all humans are capable of the level of choice or awareness that is required for participation, such as with research on infants, young children, and some adults with limited autonomy. This reiterates that the conceptual distinction between subject and participant is not simply a distinction between non-human and human, nor is it tied to any moral distinction between beings who can or cannot consent, since autonomous adult humans are often subjects of research. Instead, the distinction is more appropriately based on the intentional involvement of the being in question and what level of involvement they have in the study based on their data analysis type, where subjects are not intentionally involved, but participants are.

2.7 Minors

Before moving on to Chapter 3 where we will look at the case of whether fetuses are participants or subjects of research, I would like to note a possible challenge to my attempt to

make a relatively clean separation between subject and participant of research. As we have seen with the confusion about subject and participant when it comes to humans or non-humans, there is no absolute consistency or distinction between beings' abilities when it comes to capacity to consent. Minors are a special case since they are not fully developed in their capacity to understand consequences of research and that this capacity develops slowly over time and at different rates for different people. It is possible that two minors of the exact same age have vastly different abilities where one has the potential to be as fully informed and intentionally involved as autonomous adults, and the other has very little capacity at all and is in need of a lot of protection and guidance.

The step that minors take between subject and participant based on my conceptual definitions is not clean-cut or easily observable. When a minor goes from unknown involvement to knowing, intentional involvement, they would move from subject to participant, but exactly where this line occurs is different for every child and how exactly to measure it will be debatable. For this reason, it will often be appropriate to refer to minors as “participants” based on the type of research being conducted rather than a particular assessment of their ability for intentional involvement.

For example, if the research involves children between the ages of 9 and 11, who often fall into a “transitional” period of being capable of understanding long-term consequences and making health-related decisions (Hein et al., 2015, p. 2), and the research has a type 2 level of involvement requiring that they perform an active task such as writing a book report or playing a board game, then the use of the term “participant” would fairly indicate here that the minors are actively involved in the research in a way that might be intentional. If the research involves

very young minors, such as toddlers, and is performed by the researcher themselves, such as an eye exam, then there is no reasonable suggestion that this meets the criterion of intentional involvement since toddlers are unlikely to possess the capacity for those kinds of intentions, and the research is not an active task.

Conclusion

The first step in determining whether a fetus is a participant in research involving pregnant people is to clarify what it means to be a participant. As it pertains to human research, the terms “subject” and “participant” are often used interchangeably with a preference for the latter as both a sign of respect and a descriptive of the level of involvement the person has. Despite this preference for the term “participant,” there is still room for the term “subject” in both non-human and human animal research where involvement cannot be considered intentional, such as for a dog who is incapable of intentionally participating in research, and an adult who is not aware that their data is being used.

For conceptual clarity, it is important that these terms are used consistently in order to indicate the level of involvement that does take place. It would be incorrect to call a Twitter user a “participant” of research when they were unaware the research took place, and it would be disrespectful to call someone receiving a cancer treatment under review a “subject” of research when their role involves actively choosing a new health regimen and managing their medications. Most non-human animals will fall under the category of subject because they are not intentionally involved in research, but this does not mean that they can never be participants, nor does it mean that being a subject of research is harmful. When it comes to application of the conceptual terms, some guidelines like the TCPS2 choose to use the word

“participant” for simplicity and recognize that this is meant to capture the conceptual range of involvement from subject to co-researcher. This can also be a helpful tool for application so long as there is consistency in how these terms are used.

The key factor making one a participant of research instead of a subject is intentional involvement, which is related to the control that they personally have over their involvement in research. One is a subject if their data analysis is type 1 or 2 and they are unaware or not intentionally involved in research, but they are a participant if their data analysis is type 1 or 2 and they are intentionally involved. Recall that intentional involvement does not require formal consent, but that this is how it is most likely manifested in research for adults. For minors, or those who lack capacity to consent, their consent secured by an SDM does not make them intentionally involved since the intention came from the SDM and not the subject themselves.

In order to arrive at this distinction between the two terms I examined descriptive accounts of how the terms were used in policy, style guides, and published studies, as well as prescriptive accounts that gave arguments about when the terms were best used. I do not have recommendations for the use of the terms “partner” or “collaborator” beyond commending their current usage to denote involvement beyond the execution of the research.

It is important to remember that the terms “subject” and “participant” can indicate differing levels and types of involvement of research without being morally loaded terms. What I mean by this is that one does not need to be a moral person in the sense of personhood to be a participant, nor does the status of the being as a person indicate whether informed consent is required for their involvement in research. Chapters 4 and 5 will address more detail about the principles and policies involved in labelling a fetus a subject, including that of proxy

consent. Determining when consent is required for research subjects or participants is not simply a matter of the personhood status of the being in question.

Although occasionally implied in my writing, I did not adequately touch on the terms that should be used for non-animal beings such as plants, but that discussion is beyond the scope of this project, nor does my work need to address the possibility for “objects” of research such as rocks or chemicals. The history of the term “subject” coupled with the lack of consistency in the current usage of the term allowed for a conceptual confusion surrounding best practices of their use and implications of the labels, and my intentions here were only to provide clarity to this issue for the purposes of analyzing research involving pregnant people.

In Chapter 3, I will use the criterion of intentional involvement to suggest that a fetus cannot be considered a participant of research, but that there is still plenty of room for one to be considered a subject when their data is being analyzed in research. I will then examine four example cases of research involving pregnant people to determine some boundaries of the status of the fetus as a subject dependent on the type of research performed, and to look at the possibility of research taking place where the fetus is the subject, but the pregnant parent is not.

By opening up the definition of research subject to include that of a fetus in Chapter 3, and later in Chapters 4 and 5 determining when fetal subjects might require proxy consent, I am paving the way to reduce hesitancy from researchers and REBs to conduct and approve research with pregnant participants. It is my sincere hope that providing these methods for adjudicating current issues of research involving pregnant people will help increase the volume and frequency of safe, ethical, and meaningful research so that pregnant people and fetuses can

benefit from the answers that researchers can provide about health and wellbeing during pregnancy. It has been clear for decades that it is not acceptable that research during pregnancy is lacking and something needs to be done so we can rectify this issue soon.

Chapter 3- What to Expect When You're Participating

Introduction

The two central questions of my work are: *can fetuses be regarded as participants in clinical research?* and, if yes, *what ethical principles and guidelines should guide this treatment?* So far, I have addressed this question by first indicating the reason the status of the fetus is not well established, and then by exploring what it means to be a participant, or a subject more generally for beings involved in research. In Chapter 2, I concluded that subjects are beings who do not themselves agree to research, such as animals who cannot consent, or autonomous adults who are unaware their data is being used for research; and participants are beings who are intentionally involved in research, which is restricted to beings who can at least assent and when that assent or consent has been given.

To help us determine whether a being is a subject, participant, or simply adjacent to the research question, there are three types of data analysis that can determine someone's involvement in research and whether they are a subject or participant: type 1 is when one's data is produced outside of the research question – such as biobanked data for earlier research, or a tweet made for entertainment – and analyzed now for a new research question. Type 2 is a very broad range of all research conducted that produces and collects its own unique data including answers to survey questions about diet, and brain scans for cancer research. Type 3 is when no data is being analyzed in the research, therefore the being is not involved at all, but might appear to be involved because the individual is a support person or guardian of the being whose data usage is type 1 or 2 in the research, such as someone driving to an appointment, or

taking notes. These types were examined when looking at born humans including autonomous adults, adults with diminished capacity, and minors.

The next steps in this project are to apply these definitions of subject and participant to research involving pregnant people and fetuses in order to determine what this means for a fetus. Based on these definitions of subject and participant, it appears that we have answered the first question already in regards to participant status. Can fetuses *ever* be considered participants in clinical research? Without the ability to be intentionally involved in clinical research, no, they cannot be participants from a conceptual view. It is important to note here that my conceptual difference between subject and participant is not applied by the TCPS2 and is not common in Canadian research. As I will address later, all humans involved in research, whether conceptually subjects or participants, are called “participants” under the TCPS2, and therefore fetuses would be considered participants for this purpose when expanding their guidelines.

For the current purposes of my work, the question of status then moves on to the appropriate consideration of when fetuses can be subjects of research. It might seem straightforward to say that, when a pregnant person is participating in clinical research, the fetus is a subject, but that can be quickly challenged with an example outside the scope of clinical research: a survey.

If a pregnant person fills out a survey for a psychology study that asks questions about coping with the mental toll of pregnancy, but does not ask questions about the fetus, it seems that there is plenty of room for the pregnant person to be a participant of research about

pregnancy in which the fetus is not a subject. This is because the survey does not collect any data on the fetus, making their data analysis type 3.

The next assumption then would be that when fetuses are subjects of research, surely the pregnant person would be as well. However, if a parent drives their born child to a clinic so that the child can participate in research, there is no reason to believe that the parent is either a subject or a participant despite their technical “involvement” in the research because, once again, the usage of the parents’ data is simply a contact phone number or a name of a proxy, not data that will be analyzed by the study, again making their data analysis a type 3. What follows will be a discussion of how similar scenarios play out for clinical research examples involving pregnant people.

Based on the differing ways in which one can be involved in research, fetuses seem to never be capable of being participants, but they could be involved as subjects with type 1 or 2 data analysis. There is also the potential for fetuses’ data analysis to be type 3 in research pertaining to pregnancy. Although they might not have a support role like a parent or friend at type 3, the fetus could appear to be involved in the research because of their reliance on their parent’s body. Before we can determine in Chapter 4 if fetuses require consent for their involvement in research, we need to first look at these different ways that their data can be used as subjects.

In addition to determining the status of the fetus, it is important to answer the question of what role the pregnant parent might play in research since there is the possibility for the pregnant parent’s data analysis to be type 3 in research that is aimed at the health and wellbeing of the fetus and not be a subject or participant themselves. In these cases, it could increase the

possibility of the pregnant parent misunderstanding the purposes or goal of the research if their name is included as a participant when they are not the ones whose wellbeing or interests are part of the research question. When we clarify the type of data analysis and level of involvement each being in question has, we can bolster the pregnant parents' understanding of the research, and in turn, foster their autonomy in a new way.

Answering this question will help answer the question in the upcoming chapters about how the consent process should work for research regarding pregnant people. Wild & Biller-Andorno have previously suggested that parent and fetus could be regarded as a joint participant unit in pregnancy-related research (Wild & Biller-Andorno, 2016), but if the research question does not centrally consider the wellbeing of the pregnant parent, treating them as a double unit with their fetus in the research could cause the pregnant parent to believe that their data will be used more heavily, or that their interests are being studied when this is not the case. Once we determine which type of data analysis each individual has in the example cases and whether their involvement is that of a subject or a participant, we can more thoroughly discuss the merits of a joint-unit system in comparison to other options in Chapter 5.

This chapter has four sections. Each section introduces an example case of a clinical trial involving pregnant people in order to analyze the level of involvement and type of data analysis for the parent and fetus regarding the concept of participant or subject and three data analysis types outlined in Chapter 2. Sections 3.1 and 3.2 are parent-regarding cases of non-medicated eye drops and insulin-dependent diabetes respectively. The case of eye drops minimally involves the fetus because there is sufficient evidence to suggest that dry eyes and the topical

lubrication do not have an effect on the fetus' body or wellbeing, and the case of insulin-dependent diabetes has measurable involvement of the fetus because both untreated and treated diabetes during pregnancy can affect the fetus' development and wellbeing.

Sections 3.3 and 3.4 address fetus-regarding trials of Non-Invasive Prenatal Testing (NIPT) and HIV transmission prevention respectively. NIPT minimally involves the pregnant parent because it does not necessitate procedures beyond what is typical of prenatal treatment and HIV transmission prevention measurably involves the parent because it often requires medications administered to the parent orally and intravenously.

These cases serve three purposes. First, the differences between the examples show that the involvement level of the parent and the fetus is not always the same, which is why it is important to determine the status of the fetus and what role they play in the research. Second, the case examples are all based on studies that might need to occur in the near future, so they give us relevant and useful analysis for the research that might need clarity about the role of the fetus. Finally, the examples all achieve straight-forward conclusions about the role and status of the fetus and the pregnant parent, demonstrating that the clarity about the status of the fetus is achievable and a methodology can be used to apply this clarity to other cases that might arise. This brings us closer to guideline changes that can help increase the amount of safe, ethical, and meaningful research that is conducted in pregnancy to better support the health and wellbeing of fetuses and pregnant people alike.

3.1 Example Case 1: Eye Drops

Consider the use of eye drops during pregnancy for the pregnant parent. Dry eyes are a common symptom of pregnancy and they can cause irritation and discomfort but do not

commonly create lasting harm. The relationship between pregnancy and dry eyes can be due to a loss in hydration or due to a histamine response. Eye drops are a topical treatment applied to the eye to relieve this irritation.

Pregnant people are often excluded from ocular research, including eye drop studies. Since pregnancy can cause or worsen dry eyes or change one's vision, the exclusion of pregnant participants from clinical trials of eye drops is likely done with the goal of reducing cost and ensuring scientific rigor. The effectiveness of the eye drops might differ between pregnant and non-pregnant adults, meaning studies that wish to include pregnant people would need to be large enough to stratify their results into at least these two groups. With pregnancy as an exclusion criterion, the study can be conducted more quickly and cost-effectively than a more open participant group. Recent studies conducted in Denmark and Japan concluded that there is no immediate concern for negative outcomes on the fetus when the pregnant parent uses topical eye drops containing hyaluronate or diquafosol, and antazoline-naphazoline respectively (Hashimoto et al., 2021, p. 384. Thomseth et al., 2021, p. 505).

Hyaluronate is a common eye drop substance sometimes known as "artificial tears." Diquafosol promotes the production of tears as a treatment for dry eyes and is commonly used in Japan (Keating, 2015, p. 912). Antazoline-naphazoline is an antihistamine-based eye drop that can treat dry eyes caused by histamine responses such as hay fever or animal allergies (Thomseth et al., 2021, p. 505) so it goes beyond lubricating the eye and responds directly to treating the cause of dry eyes in the first place.

Because of the nature in which pregnancy affects dry eye symptoms, and the variety of eye drop substances on the market, eye drops are an under-studied treatment in pregnancy and

will require some form of targeted research going forward, making them a prime example case to use for guidelines about research. Since dry eyes do not affect the fetus, and the drops are a topical treatment also unlikely to affect the fetus, this example case can be categorized as parent-regarding, and low-involvement for the fetus.

The example is as follows: Annie is 11 weeks pregnant with one child and does not have chronic dry eye complications. She is being recruited for a Phase III trial that examines the effectiveness of hyaluronate based eye drops at all stages of pregnancy. The study is being conducted at a lab not associated with any obstetrical clinic. The study requires that the pregnant person be within 6-35 weeks of pregnancy and seeking non-medicated eye drops to treat new or worsening symptoms. Annie will need to visit the clinic, self-administer the drops as recommended, record her usage and symptoms in a daily log, and answer survey questions throughout her pregnancy about her experience.

The first question to address here is: *Is Annie a subject, participant, or something else in this study?* To answer this question, we must first look at the research question, the content of what is being studied, and whether the data was produced outside of bounds of research. The research question looks at the efficacy of hyaluronate eye drops on dry eyes caused by pregnancy. To answer the research question, the researchers will need to ask Annie questions about her symptoms, perform and review doctors' notes about her eye exams, and review her notes about the treatment she self-administers. In this case, the research question and contents under study heavily involve data that Annie produces particularly for the study itself, which places her data usage at type 2 and her as a subject. Since Annie is an autonomous adult who is capable of being aware of her involvement and her consent is legally secured for the research

to take place, she is a participant.

The next question to address is: *Is Annie's fetus a subject, participant, or something else in this study?* Since the research question focuses on the outcomes of dry eyes for Annie, and there is no reason to believe that eye drops could cause harm to the fetus, fetal outcomes are not part of the central research outcomes. In this case, if the fetus is not part of the central research question, nor is their data being analyzed by the researchers to report outcomes, their presence at the appointments only places them at type 3 and they are not a subject of the study.

Similar to the survey example, simply because Annie is pregnant does not mean that any study in which she participates also includes her fetus as a subject. It might be tempting to say that the fetus has a different status because, without the existence of the fetus, Annie would not be pregnant and therefore would not be eligible for this particular study. However, there is no relevant reason for a relationship between two beings to affect the data analysis type.

To illustrate this, consider a study that is looking to measure how youngest siblings compare in math performance against a national average. The study in question requires participants to have a particular familial relationship – at least one elder sibling – but does not require that the other person in the relationship provide any data towards the analysis or outcomes because the comparison is between the youngest sibling and an already-known national average, not between the youngest sibling and the elder(s). If Annie were to participate in this study and have her older sister Shayna in the room while she took the math test, Shayna would be present for the research appointment, and the reason that Annie is eligible to participate, but would not herself be providing any data that is analyzed by the researchers to answer the research question or produce outcomes. Just as Annie's fetus is present and relevant

to her eligibility in the eye drops study but does not need to provide data for the researchers. Both Shayna and Annie's fetus in these cases are still type 3 within the respective studies.

Let us quickly look at a modified example. It is possible that, despite eye drops being generally safe for pregnant people, this is a new study and is a first in the field, so the researchers wish to monitor and analyze fetal outcomes to report confirmation that their drops do not have any negative effects. If this were the case, since some of the data being analyzed in the study belongs to the fetus, their data analysis would then become type 2 and would also be a subject of the study, while Annie remains a participant for her own involvement and data analysis type.

What this means for general cases of parent-regarding studies with minimal fetal involvement is that there is no reason to consider the fetus a subject by default, include their outcomes in the central research question, or include their data in the overall analysis. However, due to the history of research involving pregnant people, we might see many cases in which otherwise parent-regarding research needs to include fetal monitoring for safety purposes, placing both the fetus and the parent's data analysis at a type 2 and have them each regarded as subjects or participants where appropriate.

3.2 Example Case 2: Insulin-Resistant Diabetes

Diabetes, and particularly insulin-resistant diabetes, is a major health concern during pregnancy, and. Even for those without a history of diabetes, "pregnancy is a diabetogenic state in which women have increased insulin resistance" (Zuckerwise et al., 2012, p. 439). However, this example case discusses pregnant people who have pre-existing diabetes. This is a case of parent-regarding, measurably involved fetus research since the goal of treating the

diabetes is the long-term health of the parent, but it is known that both the condition and the treatment can significantly affect the fetus.

Zuckerwise and co-authors present a case study of a 24-year-old woman in the United States with a history of diabetes mellitus that had been managed through metformin (2012, p. 439), an oral medication used to treat some cases of diabetes. However, throughout her pregnancy, the woman's diabetes became unmanageable on metformin and she was prescribed frequent and large volume injections of a standard, low-dose insulin called U-100 that she found quite difficult to maintain, resulting in health complications (Zuckerwise., 2012, p. 440). After switching her to a more concentrated insulin product called U-500, she was able to keep up the less frequent and smaller volume injections, however, as of 2012, U-500 was not well studied in pregnancy and this regimen was not often provided due to concerns over the severe negative impact of hypoglycemia (low blood sugar) that could occur (Zuckerwise., 2012, pp. 440-1).

My example case of insulin-resistant diabetes is that of the potential scenario in which one would like to conduct a randomized, active-controlled study comparing the effectiveness of U-100 and U-500 insulin during pregnancy. Considering the importance of managing diabetes, and the difficulty of frequent, large volume injections of U-100, it is not enough to conclude that the regime had efficacy in treatment, the effectiveness of the regime during pregnancy must be studied (Zuckerwise et al., 2012, pp. 441-2).

The example is as follows: Berto is 24 weeks pregnant with one child and has been previously diagnosed with diabetes mellitus that has become highly insulin resistant in pregnancy. He is now being recruited for a Phase III trial that compares the effectiveness of

U-100 and U-500 insulin injections. The study is being conducted at an on-site lab in the same building as an obstetrical clinic, although patients from other obstetrical clinics may also be recruited. The study requires that the participant be randomized into one of three treatment arms: the U-100 control, U-500 more frequent, and U-500 less frequent where less frequent requires higher volume doses per injection. Berto will need to self-inject the insulin, record blood sugar and insulin injections into a daily log, and frequently attend the lab for monitoring both during pregnancy and with his child after birth.

Again, we will begin our analysis looking at the research question and the role that Berto plays in the research. The research question in this case is the effect of different types of insulin injection on his blood sugar levels and researchers will need to review Berto's blood sugar, insulin regimen, and how closely the regimen was followed to determine how his arm of the trial has an effect on insulin-resistant diabetes in pregnancy. This is a clear case of type 2 data analysis because in order for researchers to obtain the information needed from Berto he needs to be aware of and actively involved in the intervention. Berto is a participant in the research, rather than a subject, because his data analysis is type 2 and he is an autonomous adult with the capacity and legal requirement for consent to research, which he has provided.

Although not part of the central research question, the researchers will also be analyzing the effects of Berto's blood sugar changes on his fetus and will require access to ultrasound images. Diabetes can greatly affect the health and wellbeing of a fetus and managing diabetes during pregnancy always involves including the fetus' response, even if the diabetes was chronic before the pregnancy. It is important to mention here as well, that Berto and his fetus share a blood supply, so any analysis of Berto's blood, regardless of the goal of the analysis,

will be able to show researchers some information about the fetus. What we are concerned about, however, is what researchers do with that information.

Since the collection and analysis of the data being taken from the fetus is done directly by the researchers, the fetus' data analysis is also type 2. However, unlike Berto, the fetus does not have an awareness of the situation enough to provide consent or assent, and therefore would be more appropriately considered a subject rather than a participant.

3.3 Example Case 3: Non-Invasive Prenatal Testing

Non-Invasive Prenatal Testing (NIPT) is a screening procedure performed in the first and second trimester of pregnancy to detect possible indications of chromosomal abnormalities in the fetus by examining an ultrasound and blood sample from the pregnant person and follow-up counseling about results (Zhang et al., 2015, pp. 530-1). This case is our fetus-regarding, minimally involved parent example because the goal of NIPT is to determine potential harms to the fetus, but the process of NIPT does not require procedures for the parent beyond what would routinely be performed in the context of medical care during pregnancy.

Although NIPT is a common test, it is not routine in many jurisdictions and is offered as an additional screening process, often at an additional cost. Furthermore, NIPT is relatively new, with two studies in 2008 launching its popularity (Zhang et al., 2015, p. 530). Research surrounding NIPT would therefore require pregnant participants to opt in to this supplementary screening. However, it is a minimally involved procedure for the parent because similar ultrasounds and blood tests are routine and can be performed at the same time as the NIPT test, adding very minimal inconvenience or risk to the pregnant person.

As of 2015, Zhang claimed that “clinical experience of large-scale NIPT performance in

the general population is still lacking,” despite its widescale use and indication that it would be beneficial for all pregnancies, rather than just those considered high risk (2015, p. 531). Although a lot has changed in the last nine years, studies surrounding NIPT are still needed and conducted, meaning it will be important to determine the role a fetus plays in future studies of this nature.

This example goes as follows: Carson is 13 weeks pregnant with one child. They are being recruited for a study that wants pregnant people in early weeks of pregnancy (between 11-14) to examine the accuracy of a new NIPT protocol. The study is being conducted at an obstetrical clinic and requires that Carson gives permission to the researchers to take and examine blood samples and ultrasounds that are performed by the obstetricians. The trial does require an extra vial of blood than what would routinely be taken at this time but does not require any extra imaging beyond access to their standard dating scan. Patients of the clinic enrolled in the trial will receive standard obstetrical care throughout their pregnancy and will be contacted one month after delivery to submit reports about any conditions with which their child has been diagnosed. For Carson, this is type 2 data analysis because this is new data that is needed to be provided for the study directly from Carson’s body and again, since Caron is an autonomous adult capable of consenting, their secured consent makes them a participant rather than a subject.

Like Berto, Carson’s fetus in this example also has type 2 data analysis because of the required additional blood sample being taken for the research. NIPT is considered non-invasive because no instruments need to enter the uterus or placenta, but this does not mean that no information is taken from the fetus. During pregnancy, the pregnant parent shares a blood

supply with the fetus, which is why taking Carson's blood sample is useful for screening their fetus for potential indications of medical conditions. Since the blood sample is being taken for the study and the blood is being analyzed for fetal health outcomes, the fetus' data analysis is also type 2 in the study and they are a subject.

Modifying the Case

The case of NIPT is a very interesting one and, if we modify the example, could place a parent in any of the three types of data usage depending on the exact methods and goals of the research. Since the goal of the research is to look at the health and wellbeing of the fetus, there is a potential for a NIPT trial to be performed through previously collected samples. For Carson, they are being asked to provide an additional blood sample, which places their data usage at a type 2, however, if all data could be taken from older samples, perhaps from bio-banked information that Carson had previously consented to be used for further research, their involvement in this particular study would only be type 1 and, depending on their awareness of this study taking place years after their child has been born, they might only be a subject.

It is also interesting to consider how Carson might only have type 3 data usage here, and this is where the combined physiology of the parent and fetus can complicate what it means to be a subject or participant in research. Returning to the born child analogy, the parent's body is often needed for the research to take place, but what determines whether they are involved in the research as type 1 or 2 data usage is if their data is under investigation and recorded. Looking at the blood sample part of NIPT, yes Carson's data is retained and recorded beyond information such as a name and phone number for emergency contact, but it is also worth the time to consider how this could be applied to studies in which all that is needed is an ultrasound

scan.

If the research study in question was just about ultrasound imaging to identify the gestational age of the fetus, Caron's body would be needed for the scan to take place, but in theory, Carson's information would not need to be recorded. If the researchers did not have access to the images themselves and only took down information such as the size of the fetus and whether there is cardiac activity, then the physical relationship Carson has to the research could be said to be similar to that of a parent who holds their child in their lap for an eye exam. They are present for the examination and their involvement is physical and important for the research to take place, but their data is not part of the research question or analyzed in the outcomes.

From a practical perspective, there is a very low likelihood that any research on pregnancy could take place in which the parent's health information is not needed, however. This is because the health of the pregnant parent is quite obviously linked to the health of the fetus and even something as basic as determining gestational age includes information such as last menstrual period (LMP) to be taken into consideration. So, although we could imagine a scenario in which it would be possible for the pregnant parent's data analysis to be a type 3 in research regarding fetuses, this study is highly unlikely to ever occur.

3.4 Example Case 4: HIV Transmission Prevention

When a pregnant person is HIV positive, there is a risk of them passing HIV to their child during pregnancy, childbirth, and the postpartum period, especially if they breastfeed (Connor et al., 1994, pp. 1173). Research such as the AIDS Clinical Trial Group (ACTG) 076 trials looked into treatment of HIV during pregnancy, childbirth, and breastfeeding – or more often,

required to avoid breastfeeding – with the goal of preventing this transmission, making this our fetus-regarding, measurably involved parent case.

Because of the severe effects of HIV on the human body, and the inaccessibility of HIV treatment to many people, especially in the United States, further research on the development of new treatments to prevent HIV transmission from parent to child will need to occur. It is important that research like this, where the parent is measurably involved but not central to the research question, has an adequate framework for determining the status of the fetus and the parent in order to avoid misconceptions of the risks involved and the goals of the outcomes.

As it stands, having the pregnant parent as the sole participant in research that is meant to improve the health of a fetus could lead to confusion and misconceptions about what role the pregnant parent plays in research. It would not be unreasonable for a parent in this scenario to believe that their heavy involvement in the process means they are benefitting from their involvement beyond the benefits that come from having a healthy fetus and subsequent baby. The discussion of this misconception will be illustrated further in Chapter 4.

It is also research like this HIV example that falls under the category of FDA recommendations for seeking out the “father’s” consent, which is what the researchers in the original ACTG 076 studies did. The consent forms (Appendix C) included two different formulations. First, there were two separate consent forms named “mother’s” and “father’s” and each parent – the pregnant parent and whomever was considered the father – were asked to provide consent for the pregnant parent and “baby” to be involved in the research, however the father’s consent form only specifically mentioned consent for the “baby.” The second formulation was a combined form asking for consent from both “mother” and “father.”

Recall from the introduction that this method of requesting consent effectively treats the pregnant parent as unable to provide consent for themselves. The consent forms almost exclusively mention the “baby’s” participation in research, which some could argue is a common way of referring to a fetus when pregnant, but they do also separate risks to the fetus from risks to the baby, which indicates that the forms are meant to be able the participation of born humans alone. However, since the consent process takes place at the beginning of the study, and the “father’s” consent mentions risks to the fetus, it seems that whoever is considered the father is being asked to provide consent for their baby to participate in research that is occurring involving their adult partner before their baby is born. As will be discussed further in Chapters 4 and 5, this is not an appropriate way to respect the autonomy of the pregnant parent, and it is imperative that we answer the question of whether the fetus, not just the born baby, is a subject or participant in this research, so the discussions about consent, proxy consent, and third-party involvement can be had in a way that both respects the pregnant parent’s autonomy and the fetus’ interests.

This example is modeled after the ACTG 076 trials of the early 90s that took place in the United States and France. With the goal of reducing transmission of HIV for the sake of the child that will be born, the trial required a lot of involvement from the pregnant parents. Parents were required to take an oral medication for a median of 11 weeks, and up to 26 weeks, before giving birth, have monthly sonograms after 28 weeks, undergo fetal non-stress tests weekly from week 34 to delivery, deliver in a hospital associated with the study, and bring their child for monitoring frequently for years after birth (Connor et al., 1994, pp. 1174-5). Many parents experienced adverse effects during their participation, but this was relatively equally split

between active and placebo groups, so it was concluded that the effects were likely related to labour and delivery, rather than the medication (Connor et al., 1994, p. 1177). For these reasons, this type of intervention is considered measurably involved.

It is important to note here that the goal of the research was to prevent transmission of HIV from parent to child, which means that the health outcomes of the parent's HIV were not central to the research. Parents were recruited only if they had not been recommended to take any antiretrovirals for their HIV (Connor et al., 1994, pp. 1174) and, although the medication in question was an antiretroviral which could reduce the parents' viral load, improving their health, this was not the aim of the study. Parents enrolled in the study did not receive oral medication for the two-year monitoring period after their children were born.

This example goes as follows: Deena is 18 weeks pregnant with one child, and HIV positive. She is being recruited for a Phase III study that wants pregnant people in their second or third trimester (between 14-34 weeks) to test the efficacy of a new medication to prevent transmission of HIV from parent to child against the current standard of care. The study is being conducted at an off-site lab in conjunction with obstetrical clinics and requires that participants take an oral medication through the latter part of their pregnancy, give birth in a hospital while receiving intravenous medication, and administer oral medication to their child for the first 6 months of life. Deena is also required to attend multiple monitoring sessions every two weeks after birth for the first two years of the child's life.

I will limit the analysis of Deena and her fetus' involvement in this trial to the portion of the trial that occurs before Deena gives birth. First, despite the fact that this a fetus-regarding trial and the research question focuses on the outcome for the fetus, the intervention is

administered orally and intravenously to the parent, making the data analysis type 2 for Deena. This is because Deena's data is being produced specifically for the purposes of the study and, despite the goal of the study being about the fetus' health, Deena is monitored for adverse outcomes like preeclampsia and toxic effects of the medication.

It is important to note here that, since Deena is required to take medication in this instance, there is no alternative scenario in which her data could be left out of the analysis. Unlike NIPT where we could possibly imagine a case in which Carson's data might not be needed, Deena is measurably involved in this study no matter what and, since Deena is aware of her involvement in the research and has consented to her involvement, she is a participant. Deena's fetus also has type 2 data analysis due to the non-stress test monitoring which records fetal heartbeats during movement and the monthly sonograms beyond 28 weeks of gestation, making them a subject of the research.

Conclusion

In Chapter 2, we looked at what it means conceptually to be a subject or participant and how this measures up with different types of research participation. It was concluded that, although there is no consistent set of definitions to separate subject from participant, there are descriptive and prescriptive accounts of the terms that support the need to separate them based on data analysis type and a desire to use respectful terms for humans when certain words might have an impact. From there, I developed three types of data analysis ranging from a non-involved support person to the person who is central to the research question and actively involved creating data to be analyzed. I concluded that those with data analysis types 1 and 2 who are not aware of their involvement in research should be appropriately called "subjects" and those

with data analysis types 1 and 2 who are intentionally involved in research should be called “participants.” This means that most of those with data analysis type 1 are subjects, and all of those with capacity to consent with data analysis type 2 are participants.

In this chapter, I took the three types of data analysis and their relationship to the terms “subject” and “participant” and analyzed four example cases in which pregnant people and their fetuses might have differing involvement to the research question to answer the modified central questions of *can fetuses ever be regarded as subjects in clinical research?* with a clear *yes*, and *can fetuses always be regarded as subjects in clinical research?* with a clear *no*. I have not exhausted all possible cases in which fetuses might have data usage in research through types 1-3, but the four example cases and their slightly modified versions have covered enough scaffolding for us to move forward to the second central question of this work: *what ethical principles and guidelines should guide this treatment?*

The significance of the example cases is threefold. First, it is important to show that the level of the involvement or data analysis of the pregnant parent is not always equal to that of the fetus. The case of *Eye Drops* illustrates this well, where the fetus’ data is not collected or analyzed for the research goals and, therefore, the fetus is neither a subject nor participant in the research, despite Annie, the parent, being a participant with type 2 data analysis. Furthermore, we can see that in cases like *NIPT*, sometimes the data analysis type will change based on the particular methodology in the research. This is clearly not the case for the *HIV* example, where both Deena and her fetus have type 2 data analysis and there is no way for the research to be performed otherwise.

The second significance of these case examples in particular is that each of them speaks

to a current lack of research or a need for further development, meaning that the cases could come up in near identical, or slightly modified forms in the coming years. Research on eye drops in pregnancy is lacking. There will be longstanding concerns about insulin-resistant diabetes and adequate treatment, both for those with a history of diabetes and those with gestational diabetes, until a series of effective regimes that fit differing lifestyles can be developed. NIPT is a relatively new screening process and is often undergoing research to test its effectiveness in real-world use and to develop more accurate or broader detection screening, and HIV's severe effects makes its transmission a large concern for HIV positive parents worldwide. These studies require the clarity of who is a subject, and who is a participant to determine who is required to provide consent for their participation and to clarify whose health and wellbeing is central to the research question.

Finally, by using these four case examples that show varying levels of involvement that differ between pregnant parent and fetus and speak to current needs in the research field during pregnancy, I have shown that clarity about the subject or participant can quite easily be achieved with the method of applying the three types of data analysis and the agreement-involvement to each being. Now that we have a methodology for determining who is the subject, who is the participant, and whether their data analysis is type 1 or 2, others can move on to apply this to other cases of research involving pregnant people and develop guidelines about their consent to participate. This will hopefully quell many of the worries that researchers and REBs have about research involving pregnant people so they can confidently move forward with ethical research projects that adequately capture the role of the fetus.

Until now, the discussions of consent and the consent process in research that I have

mentioned have all been descriptive accounts of how consent is normally required, or how proxy consent is often handled. In Chapter 4, I will move on to make recommendations about whether consent should be important for fetuses who are subjects of research. I argue that it is not inconsistent to require proxy consent for a fetal subject in research if we view them as a future child and want to protect their interests in a similar way proxy consent would be required for a newborn baby. However, due to the unique circumstances of the relationship between the pregnant parent and the fetus, there are also situations in which requiring proxy consent for a fetal subject is not recommended because of the potential negative consequences it could bring.

In Chapter 5, I will provide more in-depth recommendation about the policies surrounding consent for fetuses in varying situations. Chapter 5 will therefore examine the earlier posed suggestions of treating the parent and fetus as a joint type of participant where only one consent form and signature is needed for the pair as a unit. Finally, Chapter 5 will also look at what policies will need to be in place in situations where the fetus is not a subject, or consent for their involvement is not needed, such as when they have type 3 data analysis and are present, but not central to the research.

Chapter 4- Consent and Sensibility

Introduction

The two central questions of my work are *can fetuses be considered participants in clinical research involving pregnant people?* and if yes, *what are the general principles surrounding their inclusion?* To answer the first question, this project began by outlining where we were so far with the inclusion of fetuses in medical research. I have determined that fetuses can be conceptual subjects in some situations but never participants due to their inability for intentional involvement. This chapter will therefore address the new central question of *what are the general principles surrounding the inclusion of fetuses as subjects in medical research?* Following from this are two sub-questions: *Should it be required to gain consent for a fetus' involvement in research?* and *should current ethical guidelines change to account for fetal consent?* The discussion therefore includes overarching principles such as Respect for Persons and Concern for Welfare that we see in policy statements such as the TCPS2, but also the action-guiding principles that they produce such as a need for consent.

There are two main reasons why this chapter focuses on consent. Firstly, consent is a large and important part of Western bioethics, especially research ethics, and ensuring that each participant is given adequate respect for their autonomy or lack-thereof is an essential part to ensuring the research is conducted ethically. Secondly, as we have seen with FDA recommendations for including a “father’s” consent for some research during pregnancy, the role of consent in research during pregnancy has already led us down some undesirable paths. Requesting additional consent for pregnant people simply because they are pregnant, and especially when their fetuses are not considered participants, violates established ethical theory

about respecting the pregnant parent's autonomy. It is important that when making recommendations about the status of the fetus we do not fall back into this trap.

To answer the above sub questions, this chapter has five sections. Section 4.1 outlines the principle of consent and how proxy consent plays a role in research with those who do not have the capacity to provide their own consent. 4.2 examines ethical theories that support the need for consent in medical research. This includes the classics of utilitarianism and deontology as well as the Four Principles Approach specifically designed for medical ethics. Section 4.3 compares these theories to how consent is treated and justified in international ethics guidelines and the TCPS2, concluding that these guidelines adequately implement the ethical theories to cover the concerns for supporting participant consent. Section 4.4 addresses how the ethical theories and guidelines can be reasonably applied to fetal subjects through the concept of a "future child" and adherence to welfare-based support of Concern for Welfare. Finally, section 4.5 examines the four example cases and how consent could apply depending on the status of the fetus in each. The preliminary conclusion of this chapter is that requiring proxy consent for a fetus is consistent with current theories and practices in medical research and is recommended in cases like *Insulin* or *HIV* where fetal outcomes are central to the research question and the fetus is measurably involved.

In Chapter 5, we will look more closely into policy questions and changes that might need to be made to the TCPS2 in order to account for the application of these principles to the current guidelines. This is where I will introduce my co-participants model which says that the pregnant parent and fetus are individual participants where appropriate, but that their participation and health outcomes are inextricably linked. Both fetus and parent are individual

participants who have separate interests, and these interests can be shared or be in conflict, depending on the situation. As we will see in this chapter, when the fetus is a participant, the researcher has obligations to fetal interests and these should be regarded as both specific to the fetus, but also in conjunction with the pregnant parent.

Overall, the goal of this project is to provide clarity about the status of the fetus in research and to ensure that there is a straightforward way for researchers and REBs to parse out the role of a fetus in differing research contexts to hopefully reduce hesitancy for research during pregnancy and do so in a way that ensures research going forward adequately protects the interests of pregnant parent and fetus alike.

4.1 The Principle of Consent

Perhaps the most central principle guiding the involvement of research on human beings is the process of consent. Recall from Chapter 2, however, that not all subjects require consent for their participation under current ethical and legal frameworks. For example, in Canada, non-human animals do not require any consent or respect for assent or dissent through law or ethical guidelines so long as the research is not creating any unreasonable harm against them. The only time when consent would be involved is if the non-human animal is a pet. In that case, consent would not function as a proxy on behalf of the animal's best interests, but as authority over the pet as a legal owner. Also, research involving certain public information such as tweets, or national databases in certain jurisdictions such as Denmark do not require consent for their use.

Consent is the process of obtaining and maintaining a willingness to participate from the

participants that goes beyond what can be considered mere agreement or permission. That is why ethics guidelines also insist that consent be voluntary, informed, and ongoing (Canadian Institutes of Health Research, 2022, p. 32). Let us look at each of these. For consent to be voluntary, it cannot be coerced, manipulated, deceived, or bribed. It is also often described as being independent, but there is good reason to strive away from a focus on complete “independence” and isolation when it comes to decision making, since it has been argued that most decisions one makes in life are always dependent on their support and relationships within their community (Sherwin, 1998, pp. 34-5). This is especially true in pediatric settings where one’s capacity to understand and make informed decisions is constantly developing, and this development depends on their upbringing (Brother et al., 2020, p. 130). The bottom line is that the person who will be participating in the research needs to be the one to give the consent. They might find it helpful to receive advice or support from family members and experts, but it is not the family member or expert’s decision whether to consent to the research.

For consent to be genuine, it needs to be informed. This includes informing the prospective participant of the risks involved in the research, the goals and purpose of the research, what is required for participation such as medications or appointments (Canadian Institutes of Health Research, 2022, p. 36). If the prospective participant is not fully aware of the research that will take place or the risks it poses to them, then they cannot be said to have consented to it. For example, if the research will conduct two series of tests, but the prospective participant is only told about the first series, they cannot possibly be consenting to the second series of tests. This overlaps partially with the need for consent to be voluntary and free from deception, since it is not ethical for researchers to hide necessary parts of the research in order to trick the person

into giving consent.

Finally, consent must be ongoing, which means that consent at the beginning of the study can be revoked at any point and the participant has no obligation to continue with their participation. In some circumstances, this might also require the researcher to actively check in with the participants to ensure they are aware of their ability to drop out at any time, or to provide further consent throughout the process (Canadian Institutes of Health Research, 2022, p. 39).

Consent can only be given by someone with the capacity to do so. Those who cannot give consent for themselves have a designated proxy or SDM who provides consent on their behalf. Recall from Chapter 2 that proxy consent is the process in which an SDM who has cognitive capacities to provide consent for research, does so on behalf of a person who cannot provide their own consent. This can occur for young children, adults with certain cognitive disabilities, or who are temporarily or permanently incapacitated. The most common scenario is that proxy consent is provided by a close family member. For minors, this would be their parent or guardian. Under the TCPS2, only one SDM is required to provide consent for each person without their own capacity (Canadian Institutes of Health Research, 2022, p. 56).

Consent looks differently depending on the research being performed, the participant or subject in question, and the context surrounding the research. For example, medical studies that require blood samples or imaging likely involve a signed consent form with a written package that outlines the details of the tests, their purpose and risks. This would also come after discussion and explanation from a researcher. Non-clinical research such as behavioural or social studies that are conducted through an online questionnaire might only involve

checking a box that says one consents to participate after a short explanation of the purpose of the research and how the information will be used. Contact information is provided for the participant to ask more questions, if necessary, but there is no researcher ensuring each participant gave the form thorough thought or examination.

I have separated the reasons a subject might not have current legal or guideline-based requirements for consent into four main categories. 1) Consent was already given to use data produced earlier – such as biobanking where one’s biological data, like a blood sample, is stored for use later on. 2) The involvement is not considered human participation for the local jurisdiction and does not legally require consent – such as the use of public tweets. 3) The data is considered government or institutional property by local laws and does not legally require consent – such as the pharmacy data in Denmark. 4) Non-human animals are governed by different regulations around research due to their different role in society.

Let us also return to the concern of minors and other humans who do not have the capacity to consent to research that would otherwise require their consent. There are two distinct ways to view the concept of proxy consent in these cases. Firstly, one might see the proxy as fulfilling a role of substitute decision maker, where the consent being given by the proxy is meant to take the place of the consent that the subject in question is unable to provide. In this capacity, minors are required to give consent for their participation in research that does not fall under the above four categories. The issue is that they are incapable of doing so, so someone makes this decision for them as their advocate (Spriggs, 2023, p. 112).

For this concept of consent, there are also two methods in which an SDM would be expected to fulfill their role: following current or prior wishes or values and selecting what

would be in their best interest. Often, these two methods of being an SDM can occur at the same time. Minors are typically not able to fit the category of having prior wishes since they did not previously have the capacity to provide consent, but even young toddlers can express certain values that might become relevant for an SDM to consider. In that case, the SDM would more heavily need to rely on what they believe is in the best interest of the child and base their decisions on that.

For adults with dementia who once had decision making capacity, there is likely a heavier reliance on prior wishes and values that the person had expressed before they became incapable of providing their own consent and a consideration for their best interests would apply to fill in gaps that perhaps were not covered by what the SDM knows the person would have wanted (Shepherd, 2022, p. 7). For fetuses, much like newborns, the SDM would only be fulfilling the role of advocating for their best interests since they cannot form, and therefore express, wishes or values. In all cases, researchers and SDMs should both be seeking assent and respecting dissent where possible and relevant (Brothers et al., 2020, p. 131).

The second way in which one could view proxy consent is that it is not the subject's consent to give at all, but rather the SDM is being asked for consent in their capacity as authority over the child or adult who is incapable of giving consent. In this case, a parent would not be consenting to research on behalf of their child, but rather the parent would be providing their own consent to research involving their child (Varadan et al., 2021, pp. 295-6). For the purposes of this work, I consider a requirement of proxy consent to be a requirement of consent on behalf of the subject. Because of this, I do not include minors or adults with diminished capacities to be on the list of situations that do not require consent from the subject or

participant. To reiterate the conclusion that has been reached about the relationship between persons, participants, and consent: *the criteria that makes one a participant is not a necessary condition for requiring consent, whether direct or by proxy*. This is because it is possible and important to allow subjects who lack the capacity for consent an individual SDM who will act either in their best interest or with their wishes and values in mind.

Although I discuss multiple Western, and even some non-Western contexts, my intention is to focus my conclusions and recommendations on the current atmosphere of Canadian research, with one special exemption for the FDA guidelines around the “father’s” consent. To maintain this focus, I will be looking at the TCPS2 which is the main guideline for human research in Canada. Due to many similarities between the TCPS2 and other broadly endorsed ethical principles in human research, my conclusions might also be applicable to other local guidelines without significant modifications, but that is a project for another time.

4.2 Consent and Ethical Theories

The need for consent is justified by many different ethical theories. Consequentialism and deontology are two popular ethical theories that support autonomy and consent in different ways. Ultimately, the rigidity of these two theories left room for the development and adoption of pluralist accounts of ethics in medical practice and research. This is because the pluralistic accounts can capture the positives of consequence-based ethics and welfare-based ethics without the same drawbacks of picking just one theory and strictly adhering to it.

First, we will look at consequentialism, according to which the measurement of an action’s moral status is based on the consequences it produces, not the act itself. This is regardless of

whether the action itself could be seen as immoral from other theories, such as stealing, or even physically hurting someone. The most popular form of consequentialism is utilitarianism which states that actions that have consequences which bring about the most good, or utility, are the most ethical, or only ethical choice (Sinnott-Armstrong, 2023). What this means is that all consequences are evaluated based on this measure of utility, often interpreted as happiness or wellbeing, and the action that provides us with the greatest amount of wellbeing overall is the correct action to take.

An appeal of utilitarianism is that we are not restricted to strict rules about conduct when it is clear that the consequences of following those rules would not be beneficial. For example, it is often a complaint from women, or those interpreted to be women in a medical setting, that they must take a pregnancy test before medical professionals will perform certain diagnostic tests or prescribe certain medication. The usual justification behind this rule is that sometimes people will be pregnant unknowingly due to various factors and it is best to know for sure that a patient is not pregnant before putting them or their fetus at risk. However, this policy seems to indicate to patients that their healthcare providers do not trust them or their answers about whether they could be pregnant, and this lack of trust causes harm to the patient, which can be especially true for infertile patients who wish to conceive but cannot. Utilitarianism would tell us that, if health care professionals can improve overall utility by not following policy and only administering pregnancy tests when a patient agrees that one would be beneficial, then that would be the right course of action to take.

Utilitarianism can be used to justify the requirement of consent because there are multiple negative consequences that can come from performing research without one's consent. From

a societal perspective, we have already seen the negative consequences of research that has taken place in the past without proper consent procedures. A distrust in research, medicine, doctors, and scientists was formed due to the harmful atrocities of the Tuskegee Syphilis study and Nazi prisoner experimentation. Beyond the harms of the research itself, a distrust in research leads to a lack of participation, which we already know causes a large gap in scientific knowledge about the human health and the safety of certain substances. A distrust in medicine more broadly would reduce someone's willingness to seek out care when they are in need. John Stuart Mill, whose writings were an inspiration for the development of a large amount of the consequentialist theory used today, broadly supports autonomy and self-determination of individuals because doing so will uphold their interests, and therefore increase overall utility (Riley, 2006, p. 118; Mill, 2011, pp. 101-103). This in turn, supports medical autonomy and consent processes because it allows for increasing utility to achieve the best consequences.

If we look at the utilitarian view, requiring proxy consent for fetuses can still give us this benefit, or increased utility, despite fetuses lacking the capacity for self-determination or personal interests. Recall that an important aspect of consent is that it is informed. The more informed a prospective participant is about the research, the more likely they are to be in a position to give genuine consent. In some research, the fetus' wellbeing is the central question, and the pregnant parent's wellbeing is secondary or not a goal of the research at all. In these cases, having a consent process which focuses solely on the pregnant parent's consent to participate could increase the chances of confusion that they are the central subject of research or that they stand to benefit from the research question in some way. If the fetus is required to have proxy consent for these research questions, it can help to clarify for the parent that the

fetus' role is central to the research question. This also further separates the risks and benefits the fetus might face from the risks and benefits the parent might face so they are not treated as a single entity. These points will all be discussed in detail in the coming sections.

It is important to note as well that the consequentialist or utilitarian approach would not always require consent for certain research. If we look at the four typical reasons for consent not to be required, we can see that each of them likely produces good consequences without consent. For example, reason 1) is the consent had already been given earlier for use of further research on the collected data. In this case, the participants in question will not be harmed by the lack of consent to the particular research question being asked this time, and many positive consequences can come about from the use of data and its anonymization, rather than the need to collect more data or trace it back to the source for another consent process. On top of this, reason 4) is research on non-human animals, which has processes to minimize harms to the animals involved without requiring a proxy consent process for each of them. Rules about respecting dissent and reducing unnecessary pain and discomfort can achieve better consequences without requiring consent, especially when the research is designed to promote positive health outcomes for the type of animal in question. This is only to say that concluding that a requirement of consent generally produces good consequences for research and society overall does not mean that a consequentialist approach requires consent in all types of research involving all human or non-human animals.

However, this also means that a consequentialist approach to medical consent might encourage us to disregard a research participant's autonomy when it is clear that a physician or researcher can bring about better consequences by doing so. If we return to the Tuskegee

and Nazi examples, consequentialism can tell us that these studies were unethical because they brought about unethical consequences, but they cannot speak to the wrong that comes from deception or exploitation that occurred. In fact, utilitarianism could lead us to conclude that either one of these experiments were ethically acceptable if it was the case that they improved overall consequences for the population at large through an increase in medical knowledge and improved health. For potential scenarios like this, it is easy to see that consequentialism cannot always be a reliable source of protecting autonomy or requiring consent. This is why many choose to follow a deontological approach to medical consent, which focuses on respecting individuals and avoiding exploitation in all instances and not just when the consequences of exploitation are overall harmful.

Like consequentialism, deontology is a broad theory with various versions. In general, deontology states that the moral status of an action is based on a series of principles, rather than the consequences that the action produces (Alexander & Moore, 2021). The most popular form of deontology is Kantian deontology which gives us a set of principles, or maxims, to follow in regard to our actions.

The Kantian maxim most relevant to research is that we must always treat others, and ourselves, as beings with humanity and ends in themselves, and never simply as mere means to another's end (Johnson & Cureton, 2020). What this means is that we must show respect to other rational humans, their wishes, and their best interests or wellbeing. We can still use other people as means to an end in some cases, but we must do so while still respecting their humanity and not treating them as disposable (Johnson & Cureton, 2020). This is an important consideration for research contexts since those involved in research will need to be "used" by

researchers in some way or another. As we will see later, it is possible to adopt the respect-based deontological approach to research without claiming that all research is unethical so long as we ensure we are not using subjects and participants as *mere* means. Consent is the most important, and often only, way to ensure we are not treating subjects and participants as mere means, although some research contexts that do not require consent might still be respectful.

It is important to acknowledge that modern interpretations of Kantian deontology often overlook Kant's own version of what respecting humanity meant. Immanuel Kant was not speaking about all humans, but rather a very particular subset of adult white men whom he believed were the only ones capable of rational thought, and therefore, the only "persons" in question. This is supported by his statements that women are not "capable of principles" (Kant, 1764, p. 77), and that white people are the only ones who possess all necessary talents and rationality to develop intellectual pursuits (Wilson, 2014, p. 205). However, after recognizing the hateful and harmful origins of Kant's theories, we still can use them with our own interpretations going forward to apply to all humans in this case.

Treating someone as mere means is using them as an instrument to further your own goal without regard for their autonomy or wellbeing. This occurred in the Tuskegee Syphilis study when the Black "participants" of the study were not informed they were part of research, and in most cases not even informed of their syphilis diagnosis nor given any treatment (Russell, 2016, pp. 44-45). They were not given the option to decline participation or seek out treatment for their condition, and many of them suffered ill effects including death due to this. The researchers in this case did not treat the participants as persons deserving of care and respect, but rather as instruments to study for their own goals. Kantian deontology would support the

need for a consent process as a way of treating the participants as ends in themselves in a way that consequentialism cannot if it turns out that exploiting these populations could maximize utility.

However, just like consequentialism, there are drawbacks to the Kantian deontological approach. For example, public health measures are often predicated on a consequentialist approach to health care. One example of this is proof of vaccination for indoor dining during the height of the Covid-19 pandemic. This aimed at overall health improvements and ensuring that the pandemic was under some level of control, while still allowing most people to enjoy daily life. It was consequentialist by essentially coercing many people who did not want to get vaccinated into taking a vaccine and by excluding those who were not vaccinated from many social parts of life in order to improve the greater good of keeping as many people as healthy as possible. A deontological view of respect for persons, or a strict adherence to autonomy for all could not allow us to explain the benefits of public health measures that often place consequentialist benefit over individual choice.

Because of the varying benefits and drawbacks of both consequentialist and deontological approaches, many ethical guidelines follow a pluralistic approach and focus on a middle-ground in which the principles meant to be followed incorporate the need for welfare-based positive consequences and not just a focus on the individual actions that have been performed. Unlike utilitarianism, however, the welfare-based principles in a pluralistic approach like the Four Principles focuses on consequences for the individual or group relevant to the researcher, not the general population overall.

The Four Principles Approach developed by Beauchamp and Childress (1989) has far-

reaching use in Western medical practice and research and provides us with this pluralist way of combining some of the benefits of consequentialism and deontology – welfare-based and respect-based views – into a list of principles that are meant to each be fundamental in their own way. The Four Principles Approach is widely adopted in at least a modified manner. In a defense of the approach he developed with Jim Childress, Beauchamp writes that “additional interpretation and specification is needed” to develop rules from the general principles (Beauchamp, 1994, p. 147). The four principles are beneficence, nonmaleficence, respect for autonomy, and justice. They are similar to the three principles we have seen in Chapter 1 when discussing how the exclusion of pregnant people goes against adopted guidelines. The main difference here is that beneficence and nonmaleficence are separated as two separate principles whereas with the three seen in Chapter 1, it is assumed that beneficence, or a support of one’s wellbeing, sufficiently covers the principle of nonmaleficence.

The four principles are meant to be taken in a pluralistic manner where no one principle can be said to outweigh the others when they might be in conflict (Beauchamp, 1994, p. 152). For example, in medical practice, a patient might refuse a life-saving treatment when it conflicts with their cultural practices. In that case, it is not ethical for a physician to cite the principle of medical beneficence in order to save the patient’s life while ignoring the fact that forcing this treatment on the patient disrespects their autonomy which could potentially cause them harm and thus violate the principle of nonmaleficence as well. It is also true that respecting consent is important not just to satisfy the principle of respect for autonomy, but also in many cases to ensure that the patient is medically well, since a violation of one’s autonomy can have serious effects on their mental and physical wellbeing.

Built into The Four Principles Approach, therefore, is also a serious concern for consequences to the individual or group in question, although they are not the main guiding factor, and this approach supports the need for consent in research in two main ways. First: there is a need to respect the autonomy of a prospective participant by providing them with accurate information about the risks and benefits of the study and allowing them to make their own decision about whether they should be involved. Second: there is a need to ensure that the prospective participant is not needlessly harmed by the research and the best way to do that is respect their wishes about whether they are involved, or to ensure they have an advocate to do this for them. This prevents psychological harm caused by forcing them to participate as well as physical harm that might arise if they are not involved in the decision making. For example, if a researcher enrolls a participant in a study unknowingly and changes their medication, the participant in this case might not know to seek help when worrying side effects appear, or the researcher might not have all the information about the participant's allergies or sensitivities and provide a medication that harms them.

As it applies to minors, their inability to make autonomous decisions can exclude them from giving legal consent themselves, which is why they require a proxy. Merle Spriggs (2023) posits that, for minors in research, the requirement of consent is not based on a concept of autonomy, but rather Respect for Persons, and Concern for Welfare, and must come alongside the minor's assent (p. 111). Recall from Chapter 2 that assent is the concept of agreeing to proceed with the research (Kantian & Wendler, 2015, p. 461), which does not mean the minor needs to fully understand what is occurring, but rather that they must, when relevant, show a willingness to be involved (Spriggs, 2023, p. 112). Brothers and colleagues (2020) explain that

the concept of proxy consent is underlined by the understanding that minors, even newborns, will soon develop these capacities over time (p. 130) and it is best practice to involve the child in the decision making and research to whatever extent is appropriate for their stage of development (p. 131). This is supported by the UN Convention on the Rights of the Child (CRC) which frames a proxy as a way to protect a child's rights and interests, rather than to exert power or control over the child (Varadan et al., 2021, pp. 295-6).

What this means is that the requirement for consent for minors cannot always be justified through the same reasons as the requirement for consent for adults, but it is still not just one size fits all. The Declaration of Helsinki first developed the concept of proxy consent to ensure all humans had adequate protection in research regardless of their ability to consent for themselves (Varadan et al., 2021, p. 288). On this line of reasoning, we require proxy consent for newborns because they are individuals with unique needs and their interests can be best protected by having an advocate – usually a guardian – assess the situation and determine what is best for them (Spriggs, 2023, p. 112). We require proxy consent for toddlers for similar reasons as newborns, but also because they have begun to develop preferences that can be communicated, and their preferences can be best understood and respected by an SDM.

To answer the second main question of this work *what ethical principles should guide the inclusion of fetuses as subjects?* We need to determine if a fetal subject requires proxy consent. We already know that proxy consent does not always need to be predicated on some level of capacity to understand or assent, but rather can be related to individuals with unique needs that require advocacy like a newborn. If we apply this to a fetus, we will need to determine if a fetus, at least in the context of research, also has unique needs that require advocacy. Authors

such as Catriona Mackenzie, Elizabeth Harman, and Chervenak and McCollough each discuss different ways in which a fetus could be said to have interests.

Mackenzie's concept of a "future child" or Harman's "Actual Future Principle" both separate fetuses who will be brought to term from those who will not when it comes to examining fetal interests. This is also where Chervenak and McCollough's (2011) "fetus as a patient" concept can help support the view since they posit that "fetuses become patients when they are presented to a health care professional and there exist clinical interventions that are reliably expected to benefit clinically the fetus and the future child that it can become" (p. 43). This concept both relies on the idea of a pregnant parent presenting the fetus to the health care professional, since no one else can do so, and on interventions viewing the fetus as a future child.

For Harman (2000), it is the actual future of the child that matters for their interests, something we cannot know before that future comes about, but we should work within our best knowledge to ensure that fetuses whom we think we will become babies have their health protected (p. 315). For Mackenzie (1992), the deciding factor is more about the information we have surrounding the pregnant parent's uptake of parental responsibility for the fetus (p. 143), making the deciding factor whether the fetus is intended to be brought to term. Although Chervenak and McCollough separate their conceptual view of the fetus between previability and viability, they recognize that this line differs based on resources that can be accessed to ensure viability, and that this line is not useful for determining the status of the fetus since even previable fetuses can be in a fiduciary relationship with a health care professional (Chervenak & McCollough, 2011, p. 43). I will discuss the concept of fetuses not imminent to termination

and its implications in further detail in section 4.4, but for now it is important to know that fetuses conceptualized as future children have the same expectation for development of decision-making capacities as a newborn baby and it is consistent to require proxy consent for their involvement on these grounds.

The reason it is important to look back at what the ethical theories say about consent is that there is currently no Canadian standard declaring fetuses as subjects of research and, therefore, no policy dictating whether they require consent to be involved in research. If I were to focus solely on the current guidelines and what they require, I would not be able to make a statement about ethically including fetuses as subjects. The goal of this section was to show that a variety of ethical theories and principles support the need for a consent process for fetuses, should the need arise. In the next section, I will be showing how the current guidelines used by Canadian researchers, and more specifically the TCPS2, are adequate for the application of the potential changes needed for fetuses to be subjects of research requiring consent.

4.3 Guidelines and Consent

In section 4.2 we looked at ethical theories and principles which support the conclusion that when fetuses are subjects of research, there is reason to require their consent by proxy to be involved in the research process. Since we know that there are no current guidelines in Canada that require additional consent for fetal involvement, we must now determine if it descriptively consistent with the guidelines for a consent process to be required in these limited cases. This includes both the general principles and theories adopted by the guidelines to underpin their policy, as well as the detailed policy itself.

Beginning at the international level, the Belmont Report (1978) is a widely used, short document that outlines three main principles for research involving humans: respect for persons, beneficence, and justice. Written by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report is often cited as a general guideline for principles surrounding ethics in research but is not meant to replace more detailed guidelines. Written a year later, the Four Principles Approach is also meant to be a starting point for ethical rules, not a source of the rules themselves and together they serve as fundamental beginnings to modern Western bioethics.

In addition to The Belmont Report, Canadian guidelines are influenced by the World Medical Association (WMA's) Declaration of Helsinki (2013) which has been updated occasionally and also states the need to respect persons and protect their wellbeing and rights. In Canada, the main document for ethics guidelines for research on humans is the TCPS2 which also upholds the principles of Respect for Persons, Concern for Welfare, and Justice which will be discussed in detail shortly. As we have seen with The Four Principles Approach, the three principles in the TCPS2 are meant to be a pluralistic way to combine welfare-based and respect-based principles to best serve the complex needs of ethical research. For research funded by the Tri-Council of The Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council of Canada (NSERC), and the Social Sciences and Humanities Research Council of Canada (SSHRC), the TCPS2 must be used by all researchers looking to perform research involving humans and research ethics boards (REBs) that regulate the studies. This covers a large portion of research that takes place within Canada, and especially at Canadian universities since many universities require TCPS2 compliance

regardless of funding.

In the TCPS2, Concern for Welfare lines up with what the Belmont Report and the Four Principles Approach calls beneficence and is a focus on the person's wellbeing and interests. In the TCPS2 it is presented as a way of upholding one's quality of experience physically, mentally, and spiritually and maintaining social circumstances that can contribute to health outcomes such as housing or employment (Canadian Institutes of Health Research et al., 2022, pp. 7-8). This means ensuring that risks of research are reduced where possible and mitigated by potential benefits. Concern for Welfare is also meant to be considered in conjunction with Respect for Persons where the participant, or a proxy, is given final say about what is in their best interest through the consent process (Canadian Institutes of Health Research et al., 2022, p. 8).

Concern for Welfare is a welfare-based approach to fill in any gaps where Respect for Persons might not be enough. For example, the functionalist theory of consent would say that, so long as a participant consents to the research, there is nothing unethical about performing said research (Alderson & Goody, 1998, p. 1314). From a respect-based perspective, if one has checked the boxes and ensured they showed respect for the person by obtaining their consent, the level of risk that the person consents to in proportion to the benefits they might receive is not relevant to the researcher since the person is fully informed of these risks. By supporting a principle of Concern for Welfare alongside Respect for Persons, we can ensure that not only are participants respected and have provided consent for their participation, but that there is no research designed to bring about severe and unbalance harms, regardless of what a prospective participant is willing to consent to. Some discomfort, inconvenience, or risk is acceptable, but

only if it is then countered by a potential for benefit.

Respect for Persons within the TCPS2 is meant to encompass both a respect for autonomy and respect for those with diminished autonomy which is practiced by requiring consent for participation (Canadian Institutes of Health Research et al., 2022, p. 43). The TCPS2 does not define what it means to be a person or have personhood and clearly does not rely on a concept of personhood that relies on capacity for autonomy. This is related to the concept of respect for autonomy within the Four Principles Approach, however, since the Four Principles only looks at respect for autonomy, and not respect for all persons, cannot account for the need to provide proxy consent for those with diminished autonomy without further principles applied to it. Both of these principles are deontological in nature and meant to remain in place even if negative consequences might arise from doing so.

The TCPS2 is clear that “[a]n important mechanism for respecting participants’ autonomy in research is the requirement to seek their free, informed, and ongoing consent” (Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, & Social Sciences and Humanities Research Council of Canada, 2022, p. 6). I will return to the elements of consent soon. Furthermore, extending Respect for Persons who have diminished autonomy or a reduced capacity to consent means that “involving those who lack capacity to make their own decisions to participate can be valuable, just and even necessary” (Canadian Institutes of Health Research et al., 2022, p. 7). This is the process of ensuring that the SDM who provides proxy consent for the participant with diminished capacity is authorized to do so and aware of the responsibilities that come with this role (Canadian Institutes of Health Research et al., 2022, p. 55), as well as attempting to obtain assent, or respecting dissent that

the participant might provide.

Finally, as we have seen, Justice looks at who composes the participation pool and whether any group is disproportionately benefitted or harmed overall by research design, questions, and participation. The TCPS2 focuses on fairness and equity in the distribution of benefits and burdens of research overall (Canadian Institutes of Health Research et al., 2022, p. 9). We discussed these principles in Chapter 1 in the context of including pregnant people in clinical research and they have come up again now as guiding factors for the inclusion and treatment of the pregnant participant's fetuses. If we see fetuses as their own subject pool, then it is important to ensure that fetuses are also given a fair share of research for their potential benefit. Since some research during pregnancy might be about the pregnant person alone, it is not always enough to consider whether pregnant people have justice in research. We need to consider whether fetuses do, too.

As I have stated before, there is a lot of concern for the welfare of the fetus when it comes to written guidelines of research both within Canada and elsewhere, and the aspect of Justice for the inclusion of fetuses can be partially covered by the justice of inclusion for pregnant participants. The principle that is less explored is that of Respect for Persons, and more specifically the requirement of consent that it produces. This is because gestating fetuses are put in the same category as other human biological material and are considered to be material from the pregnant parent, who would be the participant needed to consent to their use. One major reason why this is a concern for current practice is that fetuses are often treated as subjects with their wellbeing, development, and interests as central to research questions and important factors in research guidelines distinct from the wellbeing, development, and interests

of the pregnant parent, and this is not the case for other biological human material.

Because consent is such an involved process most of the time, there are rules that outline who can give voluntary, informed, ongoing consent for themselves and who might lack this capacity and therefore require an advocate or representative to provide consent for them. This is where the concept of proxy consent comes in. Recall that a proxy is a person who is authorized to make medical decisions on behalf of someone who is incapable of these decisions themselves, whether this be partially, wholly, temporarily, or permanently. Two examples of this are when the person is a minor who still has not fully developed their capacity to understand the risks and consequences of something like medical research, or an adult with a cognitive disability that permanently diminishes this capacity, but other situations could require a proxy.

Like Brothers and colleagues (2020), the TCPS2 emphasizes that minors, among others who have an underdeveloped capacity to consent to research, must still be respected for the capacities that they do have. Articles 3.9 and 3.10 of the TCPS2 outline the steps researchers must take to ensure that minors are adequately respected including, seeking out an “authorized third-party” who is not in conflict of interest with the research to provide fully-informed consent on behalf of the minor, while also ascertaining the capacity for the minor to understand and assent or dissent to the research once consent has been granted (Canadian Institutes of Health Research et al., 2022, p. 56). Although assent is not sufficient in absence of third-party consent, dissent is enough to overrule third-party consent, which is in line with Respect for Persons even for those who do not fit the view of autonomous beings.

The TCPS2 also ensures that a balance is maintained for the overall inclusion of minors as

a group. Since minors usually lack deliberative decision-making capacity, they were labelled as a vulnerable group. This labelling is also important as a way to acknowledge that there have been historical examples of exploiting minors' lack of capacity such as with the Willowbrook Hepatitis Study where minors staying at a state-run boarding school for disabled children were deliberately infected with hepatitis in order to study the viruses that caused the disease from 1956 to 1970 (Munson, 2004, p. 38). Parents were asked for their consent on behalf of their children, but since the children were living at the school, parental awareness of the study and conditions was minimal. There have been many ethical concerns raised about deliberately infecting children and involving them in research without potential for benefit to them even after the study was completed (Munson, 2004, p. 39). This also points to concerns with targeting disabled minors in particular and ones that are removed from their parent.

However, after labelling minors as vulnerable in order to protect them from harms such as the Willowbrook study, there was also the unfortunate side-effect that research on much-needed information about children became hard to perform. The TCPS2 demands that researchers and REBs ensure that the research being performed requires the participation of children for its conclusions, and that children are benefitting from research and not being unfairly excluded from situations where research on adults is insufficient (Canadian Institutes of Health Research et al., 2022, p. 70). In Chapter 5, I will discuss how this same concern for Justice for fetuses as a participant group can be applied.

This theme of balancing protection and respect is reflected as well in the Belmont Report, which is less detailed and actionable than guidelines like the TCPS2, but still provides the same general guidance of ensuring that a child's desire to participate in or turn down research is

respected to the greatest capacity at which they are capable of understanding and indicating their desires (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979, p. 13). The Declaration of Helsinki does not specifically mention children, but article 28 outlines the need for an “authorized representative” of those who are incapable of giving informed consent, the need for assent, and the necessity of ensuring the research is beneficial to the participant in question either directly, or to their group with minimal risk to themselves (World Medical Association, 2013).

In this section I have shown that the TCPS2 guidelines reflect the major ethical principles and guidelines such as the Belmont Report that are of concern for researchers. This includes both welfare-based and respect-based principles and ensures a pluralistic approach so that no principle can be said to outweigh or overrule the others in all cases. For this reason, I will be applying the guidelines of the TCPS2 to the case of fetuses and see what they produce. The significance of this is that the TCPS2 should not need to make radical changes to its underlying ethical stance, including the three principles, nor its overall policy about subjects and participants, but rather open room for the inclusion of fetuses as conceptual subjects in a similar way to the inclusion of children. For the TCPS2 that would mean labelling fetuses as participants since they do not parse out the conceptual difference between subjects, participants, partners, or other roles of involvement that we saw in Chapter 2. The details of policy changes for the TCPS2 will be discussed further in Chapter 5.

4.4 Proxy Consent for a Fetus

Currently, gestating fetuses are covered under the TCPS2 in the same category as fetal tissue

and other human biological material from living or deceased humans, and they are not considered participants or subjects of research. However, their involvement in research is different than that of extracted tissue where the participant in question is the person from whom the tissue is extracted. This is seen in the fact that the gestating fetus' interests are still considered to be important considerations for the researchers (Canadian Institutes of Health Research et al., 2022, p. 69), especially when fetal health is a central research question.

What we have seen so far is that there are ethical theories more generally, and Canadian research guidelines more specifically, that lead us to the conclusion that consent is an important and necessary process for research involving humans from both welfare-based and respect-based views. Since fetuses can be considered subjects of research at least some of the time, and there are important consequences and values to be upheld for them in addition to the current standard focusing on born humans, these theories and guidelines are consistent with the need of considering a consent process for fetuses involved in research.

It is important to note here that the current rules surrounding consent, assent, and dissent for those with diminished capacity apply to scenarios where consent is required for research in general. If we return to the ways in which someone could be involved in research, there are many forms of research with human subjects that do not legally, nor ethically, require explicit consent for the research in question. This means that the question of whether the fetus requires proxy consent for their involvement in research only begins at the point where any other human subject would be required to consent as well.

In order to determine where the lines of consent might be drawn for fetal involvement in research, let us first begin with justifying why consent for a fetal subject might be required

despite no similar requirement for non-human subjects. Catriona Mackenzie (1992) introduces the concept of a “future child” to the conversation about fetal interests. She claims that when one commits to bringing a fetus to term, they have assumed a parental responsibility for the fetus as a future child that they will nurture for a long time (p. 6). By making this commitment and assuming this responsibility, the pregnant parent is also providing the fetus with a moral status that other fetuses do not possess (Mackenzie, 1992, p. 8).

Mackenzie’s argument about future children does not state that all fetuses have moral status, nor does it rely on a concept of potentiality. Instead, she accepts that fetuses likely have some claim to moral protection (Mackenzie, 1992, p. 140) and that their moral status is evolving through the gestational process, even if they can never be said to be full moral persons before their birth (Mackenzie, 1992, pp. 146). This is because, for Mackenzie, the fetus’ status is relational to the pregnant parent and birth becomes a morally significant process where the baby gains full moral status (Mackenzie, 1992, p. 143). Before that, the relational status of the fetus means that their moral status is determined by the pregnant parent and the relationship. When the parent takes on a parental commitment to the fetus, they take on a moral responsibility to protect their wellbeing, but never to the point that the parent must give up their own bodily autonomy to fulfill this responsibility (Mackenzie, 1992, p. 147).

Mackenzie’s parental responsibility argument is similar to Elizabeth Harman’s (2000) Actual Future Principle which looks at whether a fetus will be brought to term but relies on assigning moral status based on the actual future that comes about. With Harman’s view, we cannot tell today whether a fetus will have an actual future since the status is not based on whether it is intended to be brought to term, but whether it is born and becomes a moral person

(p. 318). However, our decisions about whether to treat the fetus as a being whose wellbeing and development should be protected comes from our best knowledge about the fetuses' future and whether their death is imminent (Harman, 2000, p. 319).

It is important to note here the different steps that occur, and which responsibilities are relevant for the parent and researcher. Both Mackenzie and Harman hold the strong view that a pregnant parent does not have the obligation to commit their body to the growth of the fetus. This means that the use of the pregnant parent's body for fetal growth is a choice that the pregnant parent makes for themselves. However, they do both make claims that, so long as the pregnant parent does choose to commit their body to the fetus, they have responsibilities to ensure the fetus' interests are cared for. Mackenzie presents this as parental commitments to long-term wellbeing (Mackenzie, 1992, p. 141) and Harman presents this as an obligation to protect the interests of a being with a future (Harman, 2000, p. 319). Neither author present the option for pregnant parents to choose to continue a pregnancy while also disregarding the fetus' interests as a future child. McCullough and Chervenak (1994) point out that this attendance to care of future interests is not special to fetuses, since all interests are "future-oriented by definition" (p. 101) and meant to deal with future concerns, welfare, or development.

The responsibility that a researcher has to a fetus is therefore dependent on whether the fetus can be said to be a future child. In situations where a pregnant parent has committed themselves to bringing the fetus to term – which is the vast majority of research involving pregnant people – the researcher is then presented with a fetus who is a future child and, as such, has future interests that the researcher is obligated to protect as they would for a born child. This is also why the researcher should see the role of an SDM for fetuses as that of an

advocate for the interests of the fetus, rather than as an authority who is providing permission for use of the fetus as property. Since the fetus is a future child, their interests are in need of protection. The researcher is not obligated to protect the interests of a fetus imminent to termination because that fetus does not have a future, will not be a future child, and arguably in that case would not have any interests.

Although, as I have argued, moral status is not needed to determine subject or participant status in research, it is this assumed parental responsibility, or commitment to future wellbeing, that can be used as a point of departure for applying requirements of consent on a fetus that we would not apply to other subjects. Like Mackenzie, we do not need to be committed to the claim that all fetuses have a requirement for proxy consent, nor do we need to say that proxy consent is a requirement for all fetuses who are not imminent to termination. However, we can say that, in committing to the future wellbeing of a fetus who will one day become a newborn child and, given that newborn children require proxy consent for their participation in research, there can be situations in which it would be deemed appropriate to require proxy consent for fetal participation in order to protect their interests. In Chapter 5 I will discuss in detail the relevant differences between a fetus not imminent to termination and a fetus imminent to termination. For now, we will focus on fetuses not imminent to termination.

If we conceptualize fetuses not imminent to termination as “future children” whose parents have already assumed a parental responsibility for their care, then requiring proxy consent for their participation begins to appear more similar to that of a newborn than to that of a non-human animal whose proxy consent perhaps serves a different purpose. As a future child, the fetus is much like a newborn where they are unable to communicate (or even hold)

preferences or values, they have no prior wishes for an SDM to rely on, and there is no way to determine their assent or dissent from the research. Nonetheless, as beings who are capable of developing these capacities and who do have physical interests for their wellbeing in need of management, it becomes appropriate for researchers to protect their individual interests through a requirement of proxy consent. However, as we will see in section 4.5, there may be cases in which protecting fetal interests can be adequately done without proxy consent, meaning it is not always required.

In addition to the reliance on Respect for Persons, and potentially more importantly, there are many welfare-based reasons for requiring proxy consent for a fetus. First, if the fetus' best interests can be protected when their level of involvement in research is made clear by a consent process, then their welfare can be improved through this protection. This is in line with the TCPS2's principle of Concern for Welfare. If a fetus is heavily involved in research and there are risks to their wellbeing that come from participation, then a lack of a separate proxy consent form or line for the fetus could lead the pregnant parent to believe that the fetus' role is more minimal than it really is. If the pregnant parent does not believe the risk or potential benefit to the fetus is significant, they might make a different decision about the wellbeing and interests of their fetus than if they were fully aware. This means that the principle of beneficence can sometimes be best satisfied by requiring fetal proxy consent.

We have also seen that one major reason to the lack of research during pregnancy is that REBs might be hesitant to approve research where fetuses are involved but it is not clear that their interests are being adequately protected. As it stands, the interests of the fetus are mentioned in the TCPS2 as something to consider for research during pregnancy, but they are

not considered participants, so the guidelines surrounding their protection are minimal compared to that of born humans. Requiring proxy consent for a fetus when they are measurably involved in research can also help to reassure researchers and REBs that the research taking place is adequately protecting fetal interests, which means the improvements made to fetal health through the work of research can increase, therefore increasing overall welfare benefits for fetuses both involved in research and in the broader population.

Second, the pregnant parents' best interests can be protected when they understand the role of their fetus in the research as it compares to their own. Does the pregnant parent take on the brunt of the risk, but the research goals are about fetal outcomes? Does the pregnant parent need to monitor both themselves and their fetus closely, or just themselves? Will the research look for fetal outcomes at all, or is it just focused on the parent? Having answers to these questions can protect parent interests and wellbeing as well since there are some situations in which a pregnant parent might feel pressured or obligated to put their fetus' wellbeing above their own (Sheppard, 2016, p. 128), and knowing exactly how the risks to themselves compare to the benefits for the fetus can reduce potential harm that might come from this obligation.

For example, pregnancy decreases one's immune responses to viruses and, during the height of the Covid-19 pandemic, pregnant people were at an increased risk of severe harms caused by contracting the SARS-CoV-2 virus (Sunder et al., 2022, p. 867). The pregnant parent themselves could face severe harms including death (Sunder et al., 2022, p. 864), but many pregnant people were concerned mostly about the health of their fetus and potentially believed that the only concern was that Covid-19 could increase chances of miscarriage. For this reason, a pregnant parent who contracted Covid-19 might not have known to monitor their own

breathing and oxygen levels because they believed that Covid-19 would harm their fetus, not them. In the same vein, when researchers make it clear that there are risks to the pregnant parent and not just their fetus, pregnant parents might be more likely to monitor their own health, rather than just have concerns for their fetus.

Thirdly, when the pregnant parent, who will be the most likely to provide proxy consent for the fetus, has the clarity about the level of involvement and each of their roles in the research process, researchers can better satisfy the principle of Respect for Persons, since the more information that is more clearly understood, the more robust the consent is that is being given. Recall that consent must be voluntary, informed, and ongoing. A major element to informed consent is that the one to provide consent should be aware of the risks and benefits of research. By clarifying the roles of the pregnant parent and the fetus in the research and ensuring that the pregnant parent knows which risks each of them are taking on, they are better informed about the research and can provide quality informed consent. As we will see in detail in section 4.5, it is possible that pregnant parents consenting to research where they are not asked to consent for their fetus are mistaken about their role in the research and this confusion questions the validity of their informed consent.

Fourthly, if we look at the principle of Justice, we can return to the overall goal of labelling some fetuses as subjects and potentially requiring their proxy consent as one to reduce hesitation about research surrounding pregnancy and fetuses and to include more pregnant people in different types of research. Doing so will improve the requirement of justice by ensuring that pregnant people and fetuses have their fair share of research benefiting their health and wellbeing. The TCPS2 is consistent with requiring proxy consent for fetuses when

these principles are better satisfied through the use of proxy consent, but this does not mean that proxy consent is required in all cases.

Requiring proxy consent for measurably involved fetal participants is an excellent method to improve all three TCPS2 principles of Respect for Persons, Concern for Welfare, and Justice. By separating the consent for the parent from the consent for the fetus, pregnant parents can be better informed about the research to which they are being asked to consent, making informed decisions can lead to improved overall welfare for both pregnant parent and fetus, and ensuring that these two things occur can increase the amount of research conducted during pregnancy, allowing for proper justice to be served. Let us now take a look at the four example cases and how these three principles can lead us to decide whether proxy consent is needed for fetal participation in each case.

4.5 Consent and the Example Cases

With the arguments about proxy consent for fetuses in mind, let us explore the four case examples. This analysis will first reiterate the conclusions of the last chapter about when the pregnant parent is a participant or subject and when the fetus is a subject, as well as each of their data analysis types. Then, I will use this information to apply to scenarios the TCPS2 would already consider a consent process necessary were the fetus a born child. It is my stance that if the fetus is a subject of research to a relevant level of involvement that would otherwise require a born child to give consent via a proxy, then there is at the very least a need to examine the benefits of doing so for the fetus in question. By using the concepts of Respect for Persons, Concern for Welfare, and Justice and their relevant welfare and respect-based backings, I make

recommendations about whether each case should require proxy consent for involvement of the respective fetal subjects.

Eye Drops

The example case of *Eye Drops* involves Annie who is 11 weeks pregnant with a single fetus and is experiencing dry eyes as a side effect from the pregnancy. We determined that Annie is a participant in this research and her fetus is not a subject since the study is not going to be monitoring fetal outcomes. Because the fetus is not a subject in this research, and their data analysis is type 3, where their data is not collected or analyzed for the purposes of the research question, there is no need to require proxy consent. Of course, Annie's type 2 involvement in this case requires her own explicit consent as per the TCPS2 and the fact that she is pregnant would require a section within the consent forms stating that there are no known risks to her fetus.

Insulin

The insulin example involves the fetus more heavily since gestational diabetes affects the health and wellbeing of both parent and child. At 24 weeks pregnant, we determined that Berto is a participant with type 2 data analysis, and his fetus is a subject with type 2 data analysis, because the fetus' outcomes will be monitored in the study. The question then is: does Berto's fetus require a consent process to be enrolled in the study? If we are to extend how type 2 data analysis is treated by the TCPS2, the fetus would be considered a subject of human research and would, therefore, require proxy consent for their participation. The insulin study also sees the researchers briefly monitoring Berto's born child for any adverse outcomes and in that

case, the born child would also require proxy consent from Berto.

For the case of Insulin, all four reasons for requiring proxy consent for fetuses apply. First, since Berto's fetus is a future child, providing them the same respect we provide newborns as beings whose capacity for consent may one day develop means that there is reason to require proxy consent. In addition, Berto is 24 weeks pregnant and requires insulin for his own diabetes that he has had even before pregnancy. Berto and his fetus could both be harmed in different and connected ways by unmanaged diabetes, such as vision loss for Berto, kidney disease and preeclampsia which can put both their lives at risk, and pre-term labour which is a risk to the health of his fetus (Alexopoulos et al., 2019, p. 4). By providing Berto with information about how the study will affect him and how the study will affect his fetus in two separate ways, then asking Berto for consent for his own participation and secondly for his fetus' participation, we are increasing the chances that Berto fully understands the individual stakes he and his fetus have in the study that go beyond their connected body tissue.

Consider scenario A where Berto is well versed in how his diabetes affects his daily life but is unaware how his diabetes can affect his fetus and also how diabetes management needs can change due to pregnancy. Berto has heard in passing about some dangers of gestational diabetes, but his friend who also has pre-existing diabetes gave birth last year and did not mention any complications. Berto is of the opinion that diabetes can be dangerous in pregnancy, but he believes that the risks to his fetus are minimal or rare. Were Berto to be given a single consent form listing all risks to him and his fetus together and only bearing his name he might be more inclined to believe that the risk to his fetus is less than the risk to himself, since diabetes is something that affects him even when not pregnant and he has not

heard of complications from his friend. This is true even after the risks and benefits have been explained to him because he could possibly consider those as statements of liability that the researchers must present, not as anything too serious.

Now consider scenario B where Berto is aware of the risks of diabetes to his fetus but believes that his own health can be managed through his usual insulin regimen. Before being recruited for the study he is already expecting that the concern will be for his fetus' health rather than his own. He is also aware of the lack of research involving fetuses and pregnant people and has read some articles mentioning that the pregnant parent is the only participant in the research, even when the fetus is of central concern. In this scenario, were Berto to be handed a single consent form bearing only his name, he might believe that his fetus is actually central to the research and the forms are only in his name since he is the adult, and he might minimize his own role in the research as "fetus-bearer" rather than someone whose health outcomes are central to the research.

It still is completely possible that Berto and others being recruited for this study are capable of fully understanding the risks and benefits of the research to themselves and their fetuses individually. However, since the fetus is a subject and their wellbeing is greatly affected by the research, it is my recommendation that separate consent forms, or at least separate signature lines on the same form will best ensure that this understanding is clear for all prospective participants. This is scenario C where Berto has some awareness of the risk of diabetes during pregnancy to himself and his fetus. He has some awareness that pregnant parents are usually treated as the sole participant whose consent matters even in research regarding fetal outcomes. Berto reads through the risks and benefits to himself and his fetus,

and he takes note that these are presented quite separately and separate pages or forms. At the end, Berto is asked if he would like to consent to his own participation in the research and, distinctly, if he would like to consent to his fetus' participation. It is at this point that Berto questions his own assumptions about minimal risk to the fetus or his role as "fetus bearer" and rethinks the information presented. It becomes harder for him to dismiss the list of risks as liability coverage and becomes clearer that both he and his fetus will be heavily involved in the research.

Finally, when it comes to the principle of Justice, REBs might be more inclined to approve studies that have strong involvement from fetuses like this when these distinct welfare-based benefits can be made clear to them. If Berto is required to provide consent for himself and his fetus, and this process of consent involves the researchers clearly explaining the individual risks and benefits, how their health affects each other, and whose health outcomes are central to the research goal, then an REB might be more satisfied that both fetal and parent interests are adequately protected in the research and the study will receive approval, providing vital information about the functionality of insulin and diabetes during pregnancy.

NIPT

The final two example cases of *NIPT* and *HIV* are both what Maria Kreszentia Sheppard would call fetus-regarding trials where the main focus of the research is the wellbeing and outcomes for the fetus. The *NIPT* example involves Carson who is 13 weeks pregnant and will be undergoing prenatal testing as a standard obstetrical procedure but is recruited to enroll in a trial that is measuring the accuracy of a new NIPT protocol. We determined that Carson is still

a participant with type 2 involvement despite their distance from the measured outcomes because their blood is needed for the testing.

For the case of *NIPT*, the main reason to require fetal proxy consent would be the future child argument and a respect for persons. However, I do not consider this a sufficient condition for a requirement of consent. The future child concept in conjunction with the welfare-based benefits of improving the pregnant parent's understanding of the research and improving overall health outcomes and experience for the parent and fetus are what would make it required to obtain proxy consent for the fetus. Since, in this case, the fetus' involvement in research is not beyond what would be required in regular medical practice and the risk to the fetus is not beyond daily life, fetal interests can be adequately protected through the standard consent process. I am not recommending a requirement of proxy consent in this case. However, it would not be inconsistent with current guidelines, nor necessarily harmful to the parent or fetus were their consent to be requested by the researchers, but there are some drawbacks.

Let us assume that this is Carson's first pregnancy, and they are still learning about the various prenatal checkups and tests that are standard for their region. Although *NIPT* is not standard, it is a common elective screening and Carson has heard many other parents talk about it as if it were straight forward and low risk. Carson is being invited to participate in this study because they are within the gestational range for the screening, but the researchers do not yet know whether Carson has chosen to pursue *NIPT*. They are simply asking Carson to contact them if they choose to have the screening done.

Imagine then scenario A where Carson has read through their clinic's information package about *NIPT* and has chosen to proceed with the screening and is asked to provide verbal

consent before the procedure. Next, Carson contacts the researchers and enquires about enrolling in the study. Were Carson to be handed two separate consent forms, or asked to sign a second time to ensure they are consenting to their fetus' involvement in the research, they might feel like the research is more invasive to the fetus or become confused about what they missed in the information package that would have mentioned this higher risk.

Now imagine scenario B where Carson is provided one research information package that clearly states the level of risk to themselves and how this is no greater than choosing to undergo NIPT under prenatal care. Being provided with a single consent form for the involvement of both Carson and their fetus is consistent with Carson's own understanding of how the screening works and is in line with the information packages that states that the research is not providing any risk beyond the usual procedure. Despite the research being fetus-regarding, and the fetus being a subject, the bulk of the physical involvement is performed by Carson. There is no medication to be passed through the placenta to Carson's fetus, no samples taken from the amniotic sack, and no procedures that would more directly involve the fetus.

Since NIPT is similar to the processes of prenatal care, Carson is well equipped to assess the risks and benefits to themselves and their fetus without additional clarity about the role of the fetus, and having a single consent form and signature line can support Carson's understanding of the research procedures, which in turn can help protect and promote both fetal interests and Carson's interests. Since we have already seen that not all subjects of research require proxy consent, and the reason to require proxy consent for fetuses is reliant on adherence to the principles of Respect for Persons and Concern for Welfare, there is no need to require proxy consent in the case of *NIPT* despite it being recommended for *Insulin*

and other fetal research.

HIV

Perhaps the most straight forward of the examples for when consent would be required, we have the HIV trial where the research continues long after the child is born. At the very least, under the TCPS2, researchers would need to obtain proxy consent for the children once they were born. However, we still need to address the need for proxy consent of the fetus during pregnancy. In this case we have Deena who is 18 weeks pregnant and HIV positive, she is a type 2 participant, and her fetus is a type 2 subject.

For the research case of *HIV* in particular, the requirement of proxy consent appears the strongest compared to the other example cases. First, the study will follow Deena and her fetus for a couple of years meaning the fetus will become a newborn and toddler through the duration of the study and most closely fits the “future child” concept. Requiring proxy consent from the beginning is a good method to respect the fact that the fetus is part of the continuum of developing capacities for consent and will have preferences that will likely be expressed before the study is done.

When examining the welfare-based reasons for requiring proxy consent, the fact that research is quite involved with high stakes and the health of the fetus is of sole interest to the research question becomes an important factor. First, when looking at the principle of Concern of Welfare, the health and wellbeing of the fetus and subsequent baby can be best protected when Deena understands exactly how her fetus will be affected not only by the research study, but also by her HIV status and lack of antiretrovirals. Like Berto, there is a chance that asking

Deena to read and sign a consent form for her participation alone could encourage her to believe that the involvement of her fetus before birth is less than it is. This is especially true in the case of *HIV* since Deena will at one point be asked to provide proxy consent for her newborn's participation. This difference in handling between fetus and newborn might be interpreted as a difference in involvement or risk and could prevent Deena from fully understanding the role her fetus plays in the research.

Secondly, it can help Deena parse out her exact role in the research and monitor her own outcomes better much like the Covid-19 example above, better satisfying the principle of Concern for Welfare for Deena as well. In the original ACTG 076 studies there was concern that the medication could cause toxic effects for pregnant parents. Were Deena to believe that her role in the study was minimal, she might not take seriously some of the mentioned side effects of the medications, believing that they are actually effects for her fetus. This could lead her to not report feeling ill because she did not believe it could be related to the study, and then continue to suffer the ill effects.

Having a proxy consent process in this case is not only consistent with the principle of Concern for Welfare, but also Respect for Persons as it will serve to better respect Deena and support her voluntary, informed, ongoing consent by making it clear to her that her fetus is the central subject. Were Deena to be asked to consent solely for own participation in a similar way as *Eye Drops*, and were she to be led to believe that the research question has her own comfort or health as a central goal, then we could not be sure that Deena was truly providing genuine consent for the research that was taking place. This means that the principle of Respect for Persons in the TCPS2 can be better fulfilled *for Deena* by having a proxy consent process

for her fetus. It is not just about respecting the fetus as a future child.

When combining Concern for Welfare and Respect for Persons we can see that they overlap. Since Deena could be randomized into the placebo arm of the trial, her potential misunderstanding about the purposes of the research can also affect her overall welfare and ability to treat her HIV. If Deena is the only participant whose consent is required for the research, she might be led to believe that her HIV status is central to the research. This is especially of concern since, once Deena's baby is born, Deena will no longer be taking medication for her HIV, but rather will be administering it to her baby. Believing that she is central to the research could cause confusion about the stages of research and how long she will be taking the medication, possibly preventing her from seeking out care while also interfering with her ability to provide truly informed consent.

Concern for Welfare and Respect for Persons for both Deena and her fetus can both be better satisfied by requiring proxy consent in a case like *Insulin* where the risk and involvement to both pregnant parent and fetus are high and even more so in *HIV* when the research question is centered around the fetus, not the pregnant parent. This is because the pregnant parent is currently named as the only participant in need of consent and the fetus could be seen as simply a factor of pregnancy, not a being whose wellbeing is under investigation in research, and even more so not a being whose interests are more relevant to the research than the pregnant parent. By using consent forms to clarify whose interests are at stake, who takes on which risks, and where these risks and involvements overlap, the pregnant parent can be better informed about the research processes and goals and make better informed decisions about what is best for their and their fetus' health.

Conclusion

The TCPS2 is the main source of bioethical guidelines for medical research involving humans in Canada. Currently, the TCPS2 does not consider fetuses to be subjects for the purposes of their guidelines and do not require any sort of proxy consent process for the enrollment of fetuses into research. I have previously argued that fetuses can be conceptual subjects for the purposes of research even if we do not consider them persons. One major reason for this is that their health and wellbeing is central to some research questions, distinct from the health and wellbeing of the pregnant parent, which separates them from other human biological material where this is not the case.

In this chapter I argued that, given the welfare-based benefit of a consent process for fetuses, and an application of TCPS2 principles such as Concern for Welfare being best supported through a consent process, it would not be inconsistent for consent to be required for fetal subjects who data analysis is type 2. This means that the fetuses in *Insulin*, *NIPT*, and *HIV* could all reasonably be required to have proxy consent for their roles in the respective research. I gave recommendations for both *Insulin* and *HIV* to require proxy consent for their fetuses on the respect-based reasoning of separate consent forms improving the pregnant parent's ability to make informed decisions and the welfare-based reasoning to protect the interests of the pregnant parent and their fetuses. Although it would not be inconsistent to require proxy consent for *NIPT*, I recommended against it for the respect-based reason that prospective participants might have increased confusion about their role and the process were proxy consent for their fetuses to be required. What I have not concluded in this chapter is that a requirement of proxy consent is the only ethical choice for these studies.

In Chapter 5, I will be addressing more details about policy regarding obtaining this proxy consent. Recall that the FDA currently suggests researchers to seek out a “father’s” consent for research with pregnant participants when that research is for the sole benefit of the fetus (U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, 2018, p. 5). The FDA does not label the fetuses as subjects, nor does it call this a form of proxy consent. In Chapter 5, I will argue why this approach to the inclusion of fetuses as research subjects is incomplete and misguided and suggest that, despite the need for proxy consent for some fetal research, there is no situation in which an additional parent’s consent is required beyond the pregnant parent’s. This is where I develop the co-participants model to manage the status of the fetus as their own participant in a way that still links them to the potential shared health outcomes and interests of the pregnant parent, as well as to adjudicate conflict.

As we will see in Chapter 6, there are implications that come along with considering fetuses human subjects of research and adapting the guidelines for their involvement within the TCPS2. Concerns such as the impact this might have on medical treatment like abortions will be examined more closely and I will defend the use of proxy consent for fetuses despite these challenges. Ultimately, the work that has been done to show that fetuses are conceptual subjects of research, and as such their interests can be best protected through a proxy consent process will lead to the conclusion that the TCPS2 should implement these changes in expectation that doing so ensures research during pregnancy can go forward safely and ethically.

Chapter 5- Policy for an Inclusive Future

Introduction

I have argued that the status of the fetus in research involving pregnant people is conceptually that of a subject when the fetus' data is being analyzed for research outcomes. This means that the fetus is not just a factor or condition of the pregnant person, and the fetus' individual needs and wellbeing should be taken into consideration in a similar way as other subjects in these cases. For some research surrounding pregnancy, the fetus' data is not collected or analyzed, meaning the fetus is not a subject. This is true even if the research is focused on pregnancy, making it a required inclusion criterion. In research cases where the fetus is not a subject, their needs and wellbeing are already adequately protected by current TCPS2 policies and do not cause a similar issue with quasi-participant status for the fetus. I thus do not recommend any changes in these cases.

Although conceptually the fetus is a subject and we can separate this from the concept of a participant, collaborator, co-investigator, or other role that an individual might play within the research context, it is important to note that, when it comes to policy and guidelines in Canada, the TCPS2 does not make the distinction between subject or participant, and instead opts to call both of these groups "participants." Thus, going forward, when discussing the TCPS2 and policy changes that need to be made, I will be using the term "participant" to refer to fetuses and pregnant people alike.

The TCPS2 governs the conduct surrounding participants in research, and since fetuses can be considered participants of research in some circumstances, it was necessary to ensure the TCPS2 was capable of adequately governing fetal participation as well. I evaluated the

capacity for the TCPS2 to apply to fetal participants and concluded that it is well equipped for this role since its underlying principles of Respect for Persons, Concern for Welfare, and Justice are shared among varying ethical theories.

The next step in this project is to outline exactly which parts of the TCPS2 need to be modified to accommodate the status of the fetus as a participant, and to provide guidance on how the new status of the fetus affects the consent process. Currently the TCPS2 does not consider fetuses participants, but it does require that fetuses be treated in a way that supports their wellbeing. Recall from Chapter 1 that a central concern that could be holding researchers and REBs back from pursuing needed research during pregnancy is the fact that the fetus is in a quasi-participant status where there are guidelines that ask researchers to consider their interests, but nothing clearly stating what role the fetus might play. This is especially true for research projects that involve pregnant participants with general health concerns that are not related to fetal wellbeing or development. The fetus' quasi status means their individuality is not recognized under the TCPS2, but their vulnerability and wellbeing are. By answering this question of how the TCPS2 should handle fetuses as conceptual subjects of research, and participants via their specific guideline definitions, we can begin to remove this hesitancy and improve research during pregnancy for both pregnant parent and fetus.

This chapter has four sections. 5.1 addresses the current status of the fetus under the TCPS2 of "human biological material" and how that is an inaccurate and inadequate status for fetuses who are conceptual subjects of research. Section 5.2 defends more robustly why fetuses should be considered participants under the TCPS2 and examines the double unit model proposed by Verina Wild (2012). Wild's view relies quite heavily on a capacity concept of personhood to

determine participant status which, as we have seen in Chapter 2, is not an accurate understanding of the general concept of participation that encompasses conceptual subject as well. This section is where I develop what I call the co-participants model that allows for both fetus and parent to be individual participants and provide individual consent directly or by proxy for their participation but also recognizes their inherently linked health outcomes and interests.

Section 5.3 is where I propose several changes to the wording of the TCPS2 in order to account for the status of the fetus as a participant and the co-participants model. This includes separating fetuses not imminent to termination from fetuses imminent to termination, fetal tissue sample, and deceased fetuses. Finally, section 5.4 uses the arguments from Chapter 4 about fetal participants sometimes requiring proxy consent to recommend the practice of defaulting to the pregnant parent as the fetus' SDM and only ever involving a third party when the pregnant parent themselves requires a proxy.

5.1 Fetuses under the TCPS2

Currently, the TCPS2 lists fetuses, fetal tissue, and embryos within the same category as human biological material. What this means is that the person whose body hosts the fetus is the only participant in the study and any research done on the fetus is considered research done on a part of the parent, requiring the parent's consent. On the surface, this does not seem like a problematic idea. If we just look at the example of adults, adults have autonomy over their other biological material like blood samples, tissue samples, or removed organs or tumours. This means that any research done on the samples or parts removed requires the consent of the

adult from which they came, and that adult is the sole participant in the research.

However, it would be very difficult to find research questions that are centered around, or in some way involve the healthy development and wellbeing of these removed samples. So, although we could easily get on board with the idea that a pregnant parent is the first, and even sole, being whose consent is required for research on their fetus, there is a large difference with how the research is being conducted in these cases. There is also a recognition of a fetus as an individual entity with distinct needs that could even conflict with the pregnant parent when this is not the case for other human biological material. This means that placing fetuses in the same category as other biological material is inconsistent with the guidelines that govern the protection of the fetus' wellbeing and the differences in the types of research questions that are answered with their involvement.

In fact, even though fetuses are covered under the general category of “human biological material” Chapter 12 of the TCPS2 separates sections A-D of their policy for materials such as “tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, and other bodily fluids” (Canadian Institutes of Health Research et al., 2022, p. 227) from section E which pertains to “the subset of biological materials that are related to human reproduction” (Canadian Institutes of Health Research et al., 2022, p. 227) including embryos, fetuses, and fetal tissue and excludes any point in which “development has been suspended” (Canadian Institutes of Health Research et al., 2022, p. 237).

This clear separation of fetuses from other “human biological material” is likely due to some differing needs of the research question. Firstly, in sections A-D where tissue and organs would be considered, there are mentions of proper preservation and disposal of the tissue, whereas in

section E, there is mention of treating genetic disorders and “ensuring normal fetal development” (Canadian Institutes of Health Research et al., 2022, p. 239). Secondly, there are stipulations about when to avoid research involving pregnant people due to the risk of harm that is be posed *to their fetus* and the possibility of answering certain research questions without including pregnant participants. You would be hard pressed to find a situation in which a potential research study is scrapped because it has been deemed “too risky” for the wellbeing of the blood sample that needs to be taken. This is because, once the sample is removed from the participant, its treatment can no longer pose a risk to the participant’s health. Fetal participants are, by definition, still attached to the parental participant and the risks to the fetus could affect both the fetus or future child, and the parent’s wellbeing, in more ways than the psychological harm that can come when there is harm to their fetus.

The line of “ensuring normal fetal development” is the crux of the fetus-as-participant argument. Fetuses are already being recognized and treated as individual entities with individual risks of harm, unlike muscle tissue or livers which are seen as risk of harm solely to the adult participant from which they came. Furthermore, this treatment of fetuses as individual entities leads to separate, clear statements about the exclusion of a different individual (the pregnant parent) due to the *fetus*’ risk of harm even if the risk to the pregnant parent is not as great. Although it is true that any risk to the fetus is also a risk to the parent due to their unique connection, the level of risk they each face can differ, and it is common practice to consider the fetus’s risk level as more relevant than the pregnant parent’s despite the fetus not being considered a participant or conceptual subject.

Due to this interconnected risk, the TCPS2 claims that “because the fetus and the woman cannot be treated separately, any intervention to one involves an intervention to the other” (Canadian Institutes of Health Research et al., 2022, p. 240). This is an important statement to take into consideration with research involving pregnant people. Although we have seen with *Eye Drops* that an intervention to one does not always mean a direct intervention to the other, we will see in further detail in section 5.2, that Wild highlights the harm that can come from viewing fetuses as detached entities needing care and protection that is entirely separate from the needs of the pregnant parent. However, I argue that acknowledging the intertwined relationship between the pregnant parent and the fetus still does not necessitate that the fetus be excluded from the concept of a participant within the parameters of the TCPS2.

Although it is the case that the TCPS2 currently treats fetuses as having a quasi-participant status and this fact needs to change, the foundations of the document are not the problem. As I argued in Chapter 4, the principles underlying the TCPS2 are in line with international bioethical standards and general bioethical theories that support autonomy, human welfare, and justice. The significance of this is that the TCPS2 should not need to make radical changes to its underlying ethical stance, including the three principles, nor its overall policy concerning whomever it currently considers a participant, but rather open room for the inclusion of fetuses as participants in a similar way to the inclusion of children. This can be achieved with a few additions and revisions to Articles 2.1, 4.3, and their applications throughout the document. The details of these changes will be discussed in section 5.3.

5.2 Fetuses as Participants

If we begin with the example case of *HIV* and use the current TCPS2 model of participation, the pregnant parent would be the participant in the first part of the research, then once the child is born, the child also becomes a participant, and the parent is no longer actively involved in the research. Since the pregnant parent is not the focus of the research, the only difference between a fetus and a newborn child is that the pregnant parent is no longer providing data as a participant once the child is born. This makes sense when following the assumption that the pregnant parent must be a participant under the TCPS2 even when their health outcomes are not central to the research goals because their level of involvement will always be high enough that they qualify as a participant. Their body is under examination either through scans or blood and tissue samples, and their body receives the intervention in question.

What is not straightforward, however, is why the separation of parent and fetus is what begins the child's status as participant. Their body was always under examination, their blood would have been part of any blood samples taken, and the goal of the intervention was to reach them through the pregnant parent. It is not that they are newly participating in the research, it is just that they are newly participating alone. The TCPS2 even recognizes the fetus as an individual entity in their statement that "any intervention to one involves an intervention to the other" (Canadian Institutes of Health Research et al., 2022, p. 240). There would be no need to say this same thing about a tissue sample since we do not consider it an individual entity with some level of separation from the adult, despite its clear removal from their body.

To illustrate a different possibility of two participants having related health outcomes, consider conjoined twins. Unlike pregnant parent and fetus, some conjoined twins could have

similar influence on each other and not be in a situation where one is wholly dependent on the other, but the example can still help us understand that both individuals can be participants even when their data analysis or health concerns are linked. For example, for a set of twins joined at the abdomen with independent chests and heads, one twin may have a lung condition that requires research, but the other twin does not. It is the same case here that any intervention to one twin due to their lung condition is also an intervention on the other twin's body due to the nature of their attachment. However, both twins would almost certainly be considered individual participants under the current TCPS2 guidelines, which supports the case that one is a participant based on their level of involvement, not their lack of relationship to another participant.

I briefly mentioned in Chapter 1 some of the varying preliminary suggestions for how a pregnant person and their fetus could be considered participants in research. Authors like Wild and Biller-Andorno (2016) and van der Zande et al. (2016) suggest the possibility that the pregnant parent and fetus be considered a double unit or joint participant. Both these suggestions seem to imply that there are two beings in question, but that they should be considered a single participant for the purposes of data analysis, recruitment, and consent. Van der Zande et al. do not expand on their view of a joint participant so there is nothing to support my assumptions. However, Wild and Biller-Andorno do reference an earlier paper by Wild about the double unit model that I will address now.

Verina Wild argues that “a researcher who designs a study in which a pregnant woman shall participate must see her as a double unit, that is, neither only as a woman nor only as a fetus, nor both as two separate units of concern” (Wild, 2012, p. 93). Her goal here is to counter the

‘individualization’ of fetuses who are often seen as a separate or competing being with their pregnant parent and to recognize that, from a physiological perspective, the parent and fetus are a joint being and any harm brought to one affects the other. As a double unit, Wild posits that the parent is the only person within the unit and, therefore, should be the one making the decisions regarding the unit (Wild, 2012, p. 90).

Wild does not define what it means to “individualize” the fetus and does not give us a lot of metaphysical framing for her view, but the double unit model implies that the fetus and pregnant parent are one being made of two conceptually different parts. This would appear to stem from a version of the Physiological Approach to biological individuality in which the “organism” that can be identified is a “foetal-maternal holobiont” and the parent and fetus are merely parts of this (Morgan, 2021, p. 803). A holobiont is defined as a host with many species working together for a joint goal. We are meant to see them not as two beings inextricably linked, but as one unit with two interacting parts such as a human and their gut bacteria. Since the host of the parts is a person, Wild says then that is the only part that matters for the purposes of participation and consent (Wild, 2012, p. 90).

In general, the Physiological Approach to conceptualizing a fetus states that, if everything is working in unison for one overall goal, then that is one single organism (Morgan, 2024, p. 801). This can be supported either by an immunological concept where, if the body’s immune system tolerates the object, then it is part of the organism, or a metabolic one where all parts are working together to self-maintain (Morgan, 2024, p. 801). Morgan argues that the immunological approach is the more robust one and, therefore, the best one to determine if the fetus is part of the parental organism. Since the fetus is usually tolerated by the parent’s

immune system, it is part of the parental organism (Morgan, 2024, p. 803).

This is where Morgan suggests that the holobiont view could be a way to view the relationship between the parent and fetus. That neither is the main organism with one as its part, but that both are two parts of a whole called the “foetal-maternal holobiont” and they each work together to achieve the goal of maintaining the wellbeing of the holobiont, rather than just the wellbeing of the host parent (Morgan, 2024, p. 803). This is a possible interpretation of the view that Wild has adopted since seeing the parent and fetus not as individual entities of concern, but rather as a double unit seems to imply that we cannot see them as separate organisms working towards separate goals. However, it is important to remember that Wild maintains the personhood of the pregnant parent and might reject this interpretation for its downplaying of the role of the host and inability to adequately support the parents’ autonomy.

Instead of looking at a physiological approach to organisms, we can turn our attention to metaphysics which gives us four main views for understanding the relationship between parent and fetus. First is the parthood view which states that a fetus is not its own being, but merely part of the parent in the same way that a kidney or an arm would be (Finn, 2021, p. 3). On this view, there would be no reason to consider the parent and fetus double units since the fetus is merely part of the parent and adults are not usually considered double units with their kidneys.

Next is the containment view which states that the metaphysical connection between a pregnant parent and their fetus is similar to that of a refrigerator and a tub of yogurt. The yogurt is not part of the refrigerator, despite being inside it (Finn, 2021, p. 4). This would completely separate parent and fetus as two distinct beings, but then not allow us to make any statements about their clear physiological connection, which is a problem for researchers who need to

consider their related health outcomes.

A medium between the parthood and containment view is the overlap view which states that the fetus and parent are two metaphysical entities with some parts that are overlapped or shared. In this view, there are clear parts of the parent that do not belong to the fetus and clear parts of the fetus that do not belong to the parent, but there are shared parts – such as the placenta – that can be said to be parts of each being (Finn, 2021, p. 4). I have chosen to adopt this view for reasons I will explain shortly.

Wild's view seems most consistent with an “underlap” metaphysical view of pregnancy. The underlap view is a way of conceptualizing the fetus and the pregnant parent as two different beings in a way that does not fully separate them like the “containment view” might. For the underlap view, there is a part of the pregnant parent that is the container for the fetus. If the fetus is not in the container, then the pregnant parent is not missing a part in the same way as they would be missing an arm or a kidney, however, the parent is also not merely a container for the fetus, since they have other parts to them as well, unlike a refrigerator whose sole job it is to contain food (Finn, 2021, p. 5). However, as a double unit it seems unlikely that Wild would accept any metaphysical view where the fetus is merely inside a container, whether that be the entirety of the parent or just a part. We have some speculation as to what type of metaphysical or biological approach Wild is taking to the double unit, but we cannot say with certainty which one she intends to invoke, making it difficult to assess.

The benefits of Wild's double unit model come at the application stage. Wild is concerned about the misogynistic view that pregnant people are seen as incapable of making rational decisions once they become pregnant and that the fetus is an independent individual who needs

protection from harms; including protections from the irrational decisions being made by their pregnant parent. She rightly points out that there is harm done when the pregnant parent and fetus are seen as unlinked individuals and the wellness of one is not regarded in conjunction with the wellness of the other. This can lead to a hyper focus on fetal rights without consideration for the effect it has on the parent, or the assumption that the parent's body merely houses the fetus rather than intertwines with it (Wild, 2012, p. 89).

Logistically, the double unit is a seemingly simple solution to tie up loose ends. The fetus does not have status as a participant or conceptual subject, but their health outcomes are considered alongside that of the pregnant parent, and there is no confusion about who is meant to make decisions on the fetus' behalf because they are not an individual, they are part of a unit with a person who has all these rights already for them. However, despite the noble goal of ensuring pregnant people are adequately respected and included in research, Wild's argument does not give us enough reason to accept the stronger view that the fetus should never be individualized as their own participant for research purposes as the only way to avoid the potential harms that can come with individualization.

First, it is clear that parent and fetus are inextricably linked in the sense that unlinking them would either cause the death of the fetus if done at an inappropriate time or change the linguistic status of the fetus to that of a newborn baby, and the pregnant parent into just a parent – or back to just a parent if this is not their first child. This is of importance especially given the research context where the fetus in question is not imminent to termination. So, although there is a point in time in which it is possible, and indeed prudent, to unlink a fetus and a pregnant parent, once that unlinking occurs, there is no longer a fetus nor a pregnant parent to

speak of. However, age alone does not make two beings into one.

The metaphysics behind pregnancy is a complicated matter, even for metaphysicians. Finn argues that, given the field of metaphysics has developed without strong considerations for the complicated case of pregnancy in mind, it is not always appropriate to apply metaphysical standards to answer questions of who is a “part” and who is a “whole” in the parent-fetus relationship (Finn, 2021, p. 8). However, she also argues that fields such as biological individuality and philosophy of science cannot give us a satisfactory answer as well, since they rely on asking the question of whether a fetus is a part of a pregnant parent without first defining what it means to be a pregnant parent and, in the end, all answers simply beg the question of identity (Finn, 2021, p. 11).

I have chosen to adopt the metaphysical overlap view because this approach is consistent with the current treatment of fetuses in research and the framework provided by the TCPS2. Despite fetuses not being given status as participants, their interests, development, and needs are considered in a distinct portion of the guidelines, with a section of the TCPS2 mentioning how to handle research on fetuses (Canadian Institutes of Health Research et al., 2022, p. 240).

Although I will not spend time defending the general metaphysical claims of the overlap view, I briefly defend why I have chosen to adopt it and why I believe it is conceptually and practically consistent with the TCPS2. From a conceptual perspective, the pregnant parent and the fetus are two beings because we speak of them as such, we have different intended outcomes for their health, and the pregnant parent themselves could see the fetus as a different being inside of them, not simply an extension of the self. The fact that the fetus is quite often a “future baby” makes this conceptual distinction clearer. As parents prepare for the arrival of

a baby, they might purchase a separate bed, clothing, and even artwork for the separate being that will likely soon be able to use and enjoy those items. Many parents choose to name their fetus before birth and speak of their personality or activities as separate from their own in a similar way as they would for a born child. The TCPS2 recognizes that the fetus has its own interests and wellbeing by mentioning that these interests need to be taken into consideration without simply seeing them as inherent in the claim that the pregnant parent's interests should be protected.

From a practical perspective, the case examples of *Eye Drops* and *NIPT* show us that there are physical differences between the pregnant parent and fetus that are not always intertwined, much like the twins joined at the abdomen. For *Eye Drops* we have seen that pregnant parents are able to take topical medications that do not influence the fetus. They are processed through the parent's body in a way that does not harm or benefit the fetus beyond being linked to a more comfortable pregnant parent. With *NIPT* we have seen that there are markers in fetal blood that can indicate potential health conditions of the fetus that do not pose harms to the pregnant parent beyond worry or stress about their fetus and future child. Again, it is important to note that in order to collect fetal blood, we must collect parental blood, but this points only to the parts of their bodies that overlap, not their identity as a unit. As we will see in section 5.3, the TCPS2 also specifies that there could be instances in which one might be affected by research in a way that does not make them a participant, which is what we are seeing here with the fetus in *Eye Drops*.

From the phenomenological perspective, Young (1984) argues against the typical view of the subject and the self to present an understanding where the fetus can be an "other," while

still being the pregnant parent's body (p. 47). She criticizes views from Merleau-Ponty and others who synonymize the body with the self for not being able to account for the experience of pregnancy (Young, 1984, p. 50). This view also allows for a type of overlap perspective where the fetus and parent share a body but are still two subjects of being, while allowing us to accept Wild's insistence that the fetus not be individualized as a separate body.

The co-participants model asks us to see the fetus and the pregnant parent as two beings, two participants, who are linked. This only applies in cases where the fetus is a participant in the research, such as with *Insulin* or *HIV*. For research like *Eye Drops* where we have already assessed that the fetus is not involved in the research enough to meet the criteria of a conceptual subject, and therefore a participant under the TCPS2, there is only one participant and that is the pregnant parent. There are three benefits to the co-participants model over the double unit model. First, it does not rely on a concept of personhood. Second, it still achieves the goal of respecting pregnant parents' autonomy. Third, it helps clear up potential misconceptions about the target of the research question when the fetus is the central participant.

The first benefit of the co-participants model over that of the double unit is that it does not rely on any concept of personhood to determine participant status whether this be weaker definitions of moral community, or more robust definitions including agency. For the purposes of research, and especially for an application to the TCPS2, the determination of who is a participant is not and should not be reliant on a moral concept of personhood, regardless of where one might draw this line. The status of participant is given by the TCPS2 to all human conceptual subjects and participants of research and applies to all humans regardless of their ability to provide consent for themselves (Canadian Institutes of Health Research et al., 2022,

p. 31). The co-participants model is consistent with this and does not bring in any view of personhood to determine participant status. This leaves out discussions of legal personhood or cognitive capacity, which would be more appropriate for the application of consent, rather than the status of participant.

The second benefit of the co-participants model is that it can still leave room to achieve the same goals Wild sets out to achieve with ensuring that the pregnant parent is the only one providing, refusing, or withdrawing consent for both parties. As I will argue in detail in section 5.4, even if we were to require proxy consent for the fetus under some circumstances, the most appropriate person to provide that consent for the fetus is the pregnant parent themselves. There is no reason in which researchers should be required to seek out consent from a second parent, or to question the pregnant parent's ability to provide consent for their fetus outside of typical circumstances in which a potential participant's consent might not be valid. Cases in which the pregnant parent is too young, cognitively disabled, or incapacitated in a way that makes them unable to provide consent for themselves would be the only scenario in which consent for their fetus would need an additional person involved. It is also important to note here that research conducted on pregnant parents who are unable to provide consent for themselves would be rare.

In addition to achieving this goal, the co-participants model can still maintain the logistic benefits of the double unit model. For the double unit model, the data collected for the pregnant parent and fetus would be filed under a single coded identifier and all the paperwork would be kept together since they are a single participant. With the co-participants model, it is still possible to code the data together with a system of matching or linked participant identifiers.

Instead of being one participant code with samples from two parts of the unit, which I imagine are differentiated anyway, the data can be stored as two related participant codes. Some options could be sequential numbers, or nearly identical codes but an “F” ending for fetal data.

The final benefit of reducing confusion about who is central to the research question is a benefit that makes the co-participants model not only a stronger option to the double unit model, but potentially the most preferable to any alternative model that cannot clear up this confusion. Recall the *HIV* example, where it is possible that the pregnant parent believes their role in the research is greater than it is intended to be because the role of the fetus is reduced to being part of the parent. In *HIV* the goal of the research is to prevent transmission of HIV from parent to child during pregnancy, childbirth, and potential breastfeeding for the first two years of life. Due to the intertwined nature of the parent and fetus’ bodies, the study begins with antiretrovirals, or a placebo being administered to the pregnant parent. In this case, the parent can benefit from the reduced viral load beyond the benefits that might come to preventing HIV transmission to the fetus.

However, once the child is born, the study encourages all parents to forgo breastfeeding and to administer the intervention directly to the child. At this point, the parent no longer would be taking antiretrovirals and their health outcomes would no longer be needed for the study. It is clear in this case that the parent’s involvement in the research is only needed because of their physical relationship with the fetus and that the true target of the research is the fetus and subsequent child.

The double unit model would rightfully treat the parent and fetus as physically intertwined but, since it would require us to focus on the pregnant parent’s personhood as the primary being

in the parent-fetus relationship, it runs the risk of minimizing that the fetus is the true focus of research. For the double unit model, the only participant that matters is the parent, since they are the only person in the relationship. If the parent is considered the only participant, much like the current concerns with *HIV*, they would be listed on all the consent forms and documents as the only participant. This could cause the parent to take this lack of acknowledgement of their fetus as a participant as an indication that the fetus' role is less than it truly is. The double unit model then puts us in a position where we could falsely place the parent as the focus of research like *HIV* simply because they hold some status of personhood. This is why focusing on personhood to define the participant can cause problems with how a prospective participant might view the research goals.

As I have argued before, falsely placing the parent as the main focus of the research in cases like *HIV* runs the risk of the prospective participant mistaking the purposes of the research or their true risk should they become involved. Wild rightfully argues that it is important not to treat the fetus as a body floating and devoid of context, but my claim is that it is also important not to overinflate the physical relationship between the pregnant parent and the fetus in situations where the balance of risks and benefits strongly favours the fetus. Leaving the fetus out of the discussion of participation or consent to participate could give potential participants the impression that the fetus' role is smaller than it truly is, or that the potential benefit to the pregnant parent goes beyond having a healthy fetus and baby. Some pregnant participants in *HIV* might believe that it is their continuing HIV status that is central to the research.

Therefore, in comparison to the double unit, my co-participants model still gives room to recognize that the pregnant parent is the default substitute decision maker for the fetus and

their autonomy and consent is what should be prioritized above any third party such as a non-gestational parent or patient advocate, but also allows us to rightfully acknowledge that fetal outcomes are central to some research questions such as with *HIV* and the role that the pregnant participant plays differs from the role the fetal participant plays. By seeing the fetus and pregnant parent as two beings who are linked, rather than two parts of one being, we are able to clarify that sometimes the fetus is central to the research question.

For example, the risks and benefits to Deena would be listed separately from those of the risks and benefits to her fetus. The research question could be centered around her fetus, rather than Deena, and it would be clear that Deena is being asked to participate in the research because it is impossible for the study to be carried out on her fetus without her participation, not because Deena's health outcomes are central to the research.

Individualizing a fetus, a concept that is not defined, does not necessitate the denial of the connection between the fetus and the pregnant parent in research. Perhaps it is actually the lack of individualization that causes some of the issues we see with hesitancy to research since it is not always clear which protections are in place for the fetus and which are in place for the parent when the parent is the only one seen as a participant. For Canada and the TCPS2, we have moved beyond the concerns of vulnerability and blanket exclusion that Wild was aiming to fix with her double unit model and are now facing the issue of *de facto* exclusion due to uncertainty and hesitancy by researchers and REBs alike, which is why I am recommending my co-participants model.

5.3 TCPS2 Suggested Changes

To account for the changes to the status of the fetus in research, there are several textual changes I suggest should be made to the TCPS2. These are displayed together in a chart format in Appendix A showing the current TCPS2 wording and my suggested changes. I will explain each of them in detail here.

Firstly, in Article 2.1, the TCPS2 separates “a. living human participants” from that of “b. human biological materials.” (Canadian Institutes of Health Research et al., 2022, p. 13) It is my suggestion that fetuses not imminent to termination should be listed as b. after “living human participants,” and that deceased fetuses can be included in the new part c. along with other human biological material. The goal of separating fetuses not imminent to termination and deceased fetuses is to allow for research on deceased fetuses or live fetal tissue to continue where the pregnant parent is still considered the sole participant from which the tissue has been removed. This is consistent with the current TCPS2 guidelines where the definition of fetus does not include any time “in which its development has been suspended” (Canadian Institutes of Health Research et al., 2022, p. 238) and would not require further changes to procedure.

The reason live fetuses with imminent termination are also left out of this category is their involvement in research is usually in the context of research on termination procedures which means there are different implications about misunderstandings of whose wellbeing or health outcomes are central to the research question and potential harms that might come to the pregnant parent if consent for fetal participation in these cases were ever to be required. Namely, that delineating a fetus imminent to termination as a research participant and requiring proxy consent for their participation could psychologically harm the pregnant parent. This is

especially true if the parent is already in a mentally vulnerable state due to their decision to terminate the pregnancy. For the purposes of research, when a parent is seeking termination procedures their fetus should be considered imminent to termination, regardless of the actual measure of time that it will take before the procedure takes place.

Recall from Chapter 4 that the separation of status of fetuses imminent and not imminent to termination is supported by Mackenzie's distinction between fetuses as a "future child" and fetuses who are not, which relates to the parental duties and responsibilities the parent takes on for the fetus before they are born (Mackenzie, 1992, p. 143). Parental commitment to the wellbeing of the fetus as a future child provides an actionable distinction for researchers to also view the fetus as a future child and consider their long-term interests. This is supported by what Chervenak and McCullough (2011) call the "fetus as a patient," where the duties assigned to researchers are based on the role of the researcher in a fiduciary relationship with a fetus to protect their wellbeing due to "the autonomous decision of a pregnant woman to continue her pregnancy" (p. 43). Chervenak and McCullough make this statement in particular about pre-viable fetuses in order to discuss the clinical difference between pre-viability and viability, but they emphasize that a viable fetus' relationship to a researcher is also subject to the autonomous decisions by the pregnant parent (pp. 43-44).

Chervenak and McCullough (2002) also stress that pregnant parents should be made aware that their involvement in research is not an obligation they have to their fetus, nor does it mean that the parent is required to bring the fetus to term (pp. 12-13). These suggestions are important for the recruitment process of research during pregnancy, and I would also add that

pregnant participants who are seeking out termination should also be made aware that they are under no obligation to follow through with the termination if they wish to change their minds.

Secondly, it is important to indicate within the TCPS2 that a fetus is not always a participant in research involving pregnant people, therefore in the application of Article 2.1 it should be mentioned that the term “fetuses not imminent to termination” includes any gestating fetus whose pregnant parent is not currently seeking termination, and whose data or interests are relevant for research outcomes. For example, a study seeking to determine the effects of insulin regimens on gestational growth. As well as when it is mentioned that “research may involve interaction with individuals who are not themselves the focus of the research” (Canadian Institutes of Health Research et al., 2022, p. 16), wording should be changed to clarify that this includes fetuses where research questions and outcomes are focused on the pregnant individual and do not involve monitoring fetal outcomes.

The additions to Article 2.1 and its application should adequately cover the determination that fetuses are participants of research when their data analysis is types 1 or 2, where type 1 is data that was generated outside of the research context and is being newly analyzed for the purposes of the research such as bio-banked data, and type 2 is where data has been generated specifically for the particular research question. But fetuses, like any other support person or adjacently relevant individual, are not participants when their data analysis is type 3, which is when their data is not under analysis and their level of involvement is adjacent to the research question. It is not necessary to explain this concept of “data analysis levels” within the TCPS2 because it is already covered under their own wording about interaction with individuals who

are not participants. Researchers and REBs will already be familiar with this concept and are capable of applying the same concept to fetuses when prompted by the new wording.

Article 4.3 addresses inappropriate exclusion of pregnant women and the application takes into account the potential risks and benefits to the embryo or fetus. The wording of this section can be expanded to clarify that considering the potential risks and benefits is still true regardless of whether the fetus is a participant in the research project since this consideration takes place during the design of the research project. It will later be determined, based on the research question and the study design whether the fetus is a participant in the research. While the project is in development, assessing risks and benefits to a fetus can help determine if their involvement constitutes participation. As we have seen in Chapter 4, the risk level of the fetus is also an important factor to consider when deciding whether fetal participants are required to have proxy consent for their involvement, but that is not something that needs to be addressed in article 4.3.

Article 12.6 addresses limits to research involving human reproductive materials, but it would also be appropriate to apply these limits to research involving fetuses not imminent to termination. Since they have been removed from the category of human biological materials, it is appropriate to create a new Article 4.7, which would occur after Articles 4.2.-4.6 about inappropriate exclusion of women, children, the elderly, and those who lack decision-making capacity. The current Article 4.7 would then be bumped to Article 4.8 and the new Article 4.7 would be modeled after current TCPS2 wording and include three main points: 1) that any research involving fetal participants should only be conducted if it can be shown to REBs that their participation is needed to answer the research question. 2) that research does not expose

fetal participants to more than minimal risk without the prospect of direct benefits to the fetus, and 3) that the fetus and pregnant parent are co-participants whose health outcomes and interests must be considered in relation to one another. It is also important to clarify here that this section is only for research where fetuses have been determined to meet the threshold for fetal participation. For fetuses with type 3 data analysis, which as you will recall means they are not involved in the study enough to warrant participant status, the guidelines will refer back to Articles 4.3 and 12.6 for research involving pregnant participants and fetal non-participants or use of fetal tissue.

In the application of Article 4.7 it will be explained that the status of co-participants means that the fetus is their own participant and in need of proxy consent, but that this proxy shall be defaulted to the co-participant pregnant parent and that the only instance in which another party would need to provide their consent for the fetus is if the pregnant parent themselves lacks decision-making capacities. It is also relevant to address here that the TCPS2 opts to use the gendered term “women” since the large majority of pregnant people are women, but it possible that researchers might come across pregnant people of other genders, and their outright blanket exclusion would also fall under the inappropriate exclusion category. I have chosen to use the term “parent” in the addition of Article 4.7 and I would urge the TCPS2 to at the very least include a footnote that any mention of pregnancy, childbearing potential, or breastfeed applies regardless of gender.

These changes to the TCPS2 cover all of the relevant changes to the status of the fetus and logistical changes to the practice of research that are needed at the guideline level. First, fetuses not imminent to termination are added as participants in the same category as living human

participants, but fetuses imminent to termination, deceased fetuses, fetal tissue, and other reproductive materials remain in the category of human biological materials that does not require the co-participants model.

Second, it is addressed clearly that not all research involving pregnant people needs to consider fetuses as participants if the data analysis type of the fetus is only 3 and their involvement is merely incidental such as a support person or parent of a born child. Finally, the question of consent for fetal participants is addressed and the co-participants model is introduced to explain that, despite fetuses being their own participants in research, they are inherently linked to another participant in all research scenarios and the co-participants model ensures that both participants either have full autonomy over their own participation or an appropriate substitute decision maker available to look out for their interests at the individual level. This ensures that pregnant parents and their fetuses alike are not inappropriately excluded from research due to concerns about risk or vulnerability.

5.4 The Consent Question

For the Canadian context, there is still the issue of determining who will be considered an appropriate SDM for the fetus' proxy consent. Wild argues that this decision lies solely with the pregnant parent since they are the only person in the double unit and, therefore, the only one who needs to provide consent for the entire unit. This is an appealing consequence of Wild's project since we have seen with the FDA's recommendation of involving a father that there are harmful implications about the parent's rights and capabilities when we ask another parent to step in in these scenarios. However, we do not need to rely on personhood or Wild's

double unit model in order to achieve this same outcome of declaring the pregnant parent the only one whose consent is needed for both co-participants.

The goal of seeking consent for the fetus is to ensure that the fetus as a participant has an adequate representative of their best interests who will be in charge of determining whether participation is appropriate for this being in particular. This is a role that can easily be fulfilled by most primary guardians at any given time. For the purposes of a pregnancy, the fetus only has one guardian: the pregnant parent. In Canadian law, the fetus is considered part of the pregnant parent for the sake of medical autonomy and, therefore, only their decisions matter for medical treatment (Reilly, 2007, p. 484). Despite the fact that the non-gestational parent in many cases will become a primary guardian upon birth of the fetus, they do not currently fulfill that role legally, nor do they have any direct role in maintaining the health and wellbeing of the fetus practically.

The only cases in which a pregnant parent would not be considered an adequate proxy decision maker of the fetus is if they are also unable to provide consent for themselves. For example, when the pregnant person is a minor, or an adult with relevant cognitive disability hindering their autonomy, they may be unable to provide informed consent and so to serve as SDM. However, even in these cases, Turnham and colleagues (2020) argue that any parent who has been deemed capable of making adequate parenting decisions should also be considered capable of providing medical consent or refusal for their born child, regardless of age (p. 359). I will address this argument further in Chapter 6 when discussing the case of consent for pregnant minors.

Even if it could be argued that the non-gestational parent is also a guardian of the fetus

before birth, the argument still favours the pregnant parent and only the pregnant parent as the SDM for the fetus under typical circumstances. First, Wild presents the double unit model as a response to the common treatment of pregnant people as a “vulnerable group” and frames the argument in favour of the pregnant parent making the decision in opposition to the claim that REBs and researchers should be the ones to protect the fetus from harm by excluding them from risky research.

In the co-participants model, there is also a strong favour of not excluding fetuses from research to “protect” them because that would go against the principles of justice and, since the fetus has status as a participant group, the principles of justice apply to them directly and not just their parents. Also, since the individual fetus has status as a participant and will be given a dedicated advocate of their interests, there is less of an argument to be made that an additional parent or an advocate needs to provide them protection since this is not something we do with any other participant. When fetuses are not participants but merely factors of consideration in research, there is no clear advocate for their interests at an individual level, which leaves room for arguments to be made that they need to be protected in aggregate by REBs through exclusion, or that a third party need to be involved.

Second, the co-participants model protects us from potential guidelines that might require a “father’s” consent such is the case with proposed FDA guidelines. The FDA does not explicitly treat the fetus as a participant of research but has a proposed guidance that does require that a “father’s” consent be sought alongside that of the pregnant parent’s in most of research aimed at solely at the fetus’ health, and we have seen this proposed guideline be implemented in real-world cases such as ACTG 076, which is what my example case of *HIV*

is modeled after. This means that researchers would not be required to seek the “father’s” consent for *Eye Drops*, or *Insulin* because they are not solely direct benefit for the fetus, but they would be required for *NIPT* and *HIV*. There are exceptions for fathers who are unavailable for various reasons, or if the fetus was conceived through rape or incest, so the requirement is not as strong as that of the pregnant parent. However, it is still something we have not seen before in any other research context, and there is room for the FDA guidelines to also expand their status of the fetus to cover these concerns. Although I will not be specifically addressing the changes needed within the FDA here, I would like to touch on some of the benefits the co-participants model can have to this effect.

The co-participants model allows for both the pregnant parent and the fetus to be participants of research when the research question is central to fetal wellbeing. Charitably, it is perhaps the clear difference between research on pregnancy aimed at the pregnant parent’s health outcomes and research aimed at fetal outcomes that has motivated the FDA’s proposed guideline. Research aimed solely at fetal health and wellbeing would most likely be research that heavily involves fetal data and could increase fetal risk. It seems that the FDA’s goal with the additional consent is to increase potential for safeguards of fetal health alongside these increases in involvement and risk.

However, as we saw with Wild’s argumentation, the requirement of consent from an additional adult for the participation of a presumably autonomous pregnant parent is a gross infringement on autonomy of the pregnant parent and a harmful assumption that they are unable to make rational choices with the best interest of their fetus in mind. The co-participants model allows us to both increase these safeguards that the FDA likely has in mind here and

prevent the pregnant parent from being treated as irrational or a threat. We can do this by recognizing that fetuses in this case are participants and their particular interests in the research context should be taken into consideration, and by ensuring that, when proxy consent is an appropriate requirement, the default person to provide that consent is the pregnant parent themselves. With the double unit model or the current practice of treating fetuses as complications in research, we cannot recognize their status as participants and governing bodies such as the FDA could be motivated to implement harmful guidelines like this that further hinder a pregnant parent's autonomy and ability to participate in valuable research.

Therefore, conflating the pregnant parent and the fetus into a single unit can have harmful implications for the pregnant parent's ability to exercise their autonomy. Although this does not occur in Wild's model since she already has a contingency for this, a joint participant model, or something similar that avoids individualizing the fetus could lead us here. In particular, this practice of seeking out a father's consent would mean that a third party has the ability to overrule the pregnant parent's consent to participate in research simply due to the fact that they are pregnant.

By blurring the lines between parent and fetus one can hide behind the claim that the father is not meant to deny the consent for the parent, but for the double unit that partially includes their DNA. If we separate pregnant parent from fetus for the purposes of consent it becomes clear that there is no reason to involve the father in the parent's consent for their own participation. It also allows us to clearly take the stand that the pregnant parent is a sufficient SDM for the other participant – the fetus – and there is no need to bring in a third party for the typical case.

A non-charitable interpretation of requiring both parents' consent for a fetus or child to participate in research is that the child is being treated like a house, or a car which cannot be sold without the permission of all legal owners, rather than a being whose lack of autonomy is being compensated for by an appropriate proxy. In typical scenarios where two parents raise a child together, it is reasonable to assume that each parent is an adequate guardian on their own. At any given point, the child could be alone with either parent and this could involve decision-making on behalf of the child ranging from which game to play to when and how much medicine to take for an illness. Although parents will discuss general rules about which decisions to make about their children, it is not common for two parents to make every minute parenting decision in tandem. Doing so would make it very difficult for the child to receive adequate care since everything from which clothes to wear to how many sprinkles of salt is too much would need to be discussed in real-time.

Since each parent can be considered an adequate guardian, they are in a position to act as SDMs for the child in the context of medical or research decisions. Regarding Respect for Persons, we can show respect to a child's, or future child's, developing cognitive capacities by ensuring they have an adequate SDM who has their best interest in mind. Regarding Concern for Welfare, if each parent is capable of promoting the child's best interests, then each parent is capable of ensuring that enrolling in research is in the best interest of the child. Finally, Justice is best fulfilled with fewer unneeded barriers to participation for under-represented populations like children and fetuses. The principles of research ethics do not require us to ask all parents or guardians for their consent to participate since the goals of these principles is to respect the participant, have their best interest in mind, and ensure they have a fair chance at

research benefits without overburden and these can be achieved by a singular parent. These same principles apply to the fetus.

Some might argue that determining that the pregnant parent is an adequate SDM still does not necessitate that they are the most appropriate SDM for the fetus since the tensions that might be faced between the pregnant parent and their fetus in the research context could lead us to prefer a more neutral party or advocate to look out for the fetus' best interests. It's important to note here that asking pregnant parents to make decisions that balance their wellbeing with that of their fetus' is not unique to research. Pregnant people face daily decisions about what they should or should not consume, what activities they participate in, or how much rest they should get that arguably place their interests in some conflict with that of their fetus'. Especially in the context of research on wanted pregnancies, pregnant parents are guardians of the fetus and have an interest in their healthy development, decreasing the chances that they will struggle to be able to adequately balance their own interests with those of their fetus. The pregnant parent is also the most obvious SDM for a fetus since they will be required to be present for any interventions involving the fetus. Pregnant parents have the most information about the fetus, the most direct access to the fetus, and the ability to adjudicate conflicting interests that another involved parent does not have, making them the first choice to fulfill the role of SDM when the question is about the fetus' best interests.

In contrast to this, were we to consider the fetus a possession, rather than a subject in need of an SDM, we might come to the conclusion that the purpose of requiring proxy consent for participation is not to fulfill the three principles from the TCPS2, but rather to obtain legal permission to perform research on this possession. Much like one cannot sell a house without

gaining permission from all legal owners, researchers would not be permitted to conduct research involving a fetus without permission from all “owners.” In this case, the assumption is that all those whose DNA went in to making the fetus would be considered an owner whose permission needs to be sought for research purposes.

With the co-participants model, I consider the fetus a participant in the same way a born child would be, not as a possession or property of the parents. My model thus better captures the ethical principles motivating the consent process. Since the default case is that all guardians of the fetus can serve as adequate SDMs and provide proxy consent for the fetus, and at present the only guardian of the fetus is the pregnant parent, then there is no need to seek out consent from any other party who may be involved in the fetus’ life once they are born. This is true even in the case of *HIV* where the research follows the fetus through toddlerhood because the born child can still be adequately represented by a single parent or guardian. It is possible that parental disagreement will occur, and that can lead to serious ethical implications. I will discuss more details of those situations in Chapter 6.

So, what does this mean for the details of the consent process? As I have said, it is still valuable to maintain the intertwined relationship between parent and fetus throughout the process, which is why I have chosen to call it the co-participants model. “Co” emphasizing that the two individuals are linked, but “participants” in plural to indicate that they still are each individual participants. Although they are two separate beings, until the fetus becomes a born child, they are wholly reliant and connected to the pregnant parent. This is especially of importance since the relevant category within the TCPS2 will only be dealing with fetuses who are not imminent to termination.

When it comes to written consent forms, it would therefore be appropriate to keep the two forms together and have each form reference the other. For research focusing on the wellbeing or development of the fetus, such as *HIV*, it would perhaps even be appropriate to place the fetus' consent form ahead of the pregnant parent's to show that the primary participant in question is the fetus. The parent's consent form could then begin with a clear statement that they are being asked to participate in this study because it is impossible for their fetus to participate without their own participation as well.

In contrast, studies like *Insulin* where the parent is the primary participant, the pregnant parent's consent form can come first, and the fetus' consent form will state that they are being asked for their fetus to participate because the intervention in question affects the fetus' health as well. Of course, in the particular case of *Insulin*, the involvement of the fetus is bordering on equal to that of the parent since insulin and glucose levels have a strong impact on fetal health and development, so it can be stated as such that the fetus is being asked to participate because they are also of central concern to the research question and outcomes.

In cases like *Eye Drops* where fetal involvement is minimal and the fetus is not a participant, it is not necessary to have a separate written consent form or information sheet for the fetus. It would be sufficient to have a few lines indicating to the potential participant that the health and wellbeing of the fetus is considered under the TCPS2 and a risk assessment has already taken place with fetal interests to determine that the risk to the fetus is minimal or negligible and no greater than the risk of everyday life, nor is the study intended to provide any benefits to the fetus.

Conclusion

To incorporate fetuses as participants into the TCPS2 and the consent process for research it is best to follow the co-participants model where both pregnant parent and fetus are considered separate participants but their recruitment, consent documents, and data analysis are linked since their outcomes greatly influence one another. Maintaining the participant status of the fetus is important in order to avoid misconceptions about which participants health outcomes are central to the research question and how the risk and benefit ratios are distributed between the co-participants. It is also preferred to use the co-participants model over the double unit model that relies on the concept of personhood to determine participant status.

The co-participants model can account for the sole consent being given by the pregnant parent through the understanding that any proxy consent given for the fetus need only to come from a suitable advocate and that the fetus' guardian – the pregnant parent – is by default an appropriate SDM in this case. It is not necessary to rely on models that reduce the fetus' status and deny their participation in order to preserve the autonomy of the pregnant parent over decisions made about their own body, including anything connected to their fetus.

With the co-participants model each participant could either have a separate written consent form that clearly outlines their individual role in the research, or a combined form with two signature lines that still delineates their separate roles. Whether that means they are the primary participant and central to the research question, or they are a participant solely because it would be impossible to conduct the research on the other co-participant without their participation as well. Consent forms will reflect the level of involvement and data analysis that is needed from each co-participant and their potential risks and benefits.

This chapter provided several recommended changes to the TCPS2 in order to account for the conclusions of the previous chapter. First, one major motivation for the lack of research in pregnancy is that REBs are hesitant to approve research when it is not clear that fetal interests are properly protected. Second, a central way to reduce this hesitancy is to determine the status of the fetus in research. Third, by examining the definitions and use of the concepts of subject and participant in research we can conclude that fetuses are conceptual subjects but should be considered participants under the TCPS2. Fourth, as participants whose interests matter to the researchers, proxy consent is often an appropriate method for ensuring these interests are considered and protected, as well as promoting the interests and autonomy of the pregnant parent. Changes to the TCPS2 to account for the status of the fetus only need to be minimal and will clarify the role of the fetus for varying levels of involvement and research types.

In Chapter 6 I address potential objections to my work including the perception that changing the status of the fetus in research will lead to the unwanted outcome of preventing essential reproductive healthcare such as termination. I will also examine how cases of surrogacy, parental disagreement, and pregnant minors can affect the proxy consent process for fetal participation.

Chapter 6- Implications and Objections

Introduction

I have argued that, from a conceptual standpoint, fetuses can be subjects in research when their data is produced and analyzed for the research question. As it pertains to the TCPS2, that would mean that fetuses, and not just their gestating parent, would be considered “human participants” and potentially awarded requirements of proxy consent for their involvement in research, depending on the details of the study and what is required to protect fetal interests. In this Chapter, I will examine some potential or perceived implications to labelling fetuses as conceptual subjects, or participants under the TCPS2. One potential implication in particular stands as an objection to taking this leap forward: the status of the fetus in regards to abortion. As we have seen, currently the TCPS2 includes fetuses in the same category as “human biological material” and only includes born humans as participants (Canadian Institutes of Health Research et al., 2022, p. 16). However, unlike other forms of human biological material, the TCPS2 pays careful attention to the wellbeing and development of the fetus and their ability to thrive after birth. This places them in a quasi-participant status where they are not explicitly participants of research but are individual human beings with interests that are considered in research contexts.

I argued that this is an unacceptable position. Chervenak and McCullough (2011) emphasize that not recognizing the status of the fetus can lead to cases of exploitation of either fetus or parent in order to provide better care for the other (pp. 39-40). As we have seen with the FDA, lacking status for the fetus and guidelines to deal with their consent can lead to requiring a “father’s” consent for participation during pregnancy, which is not an acceptable

outcome. Furthermore, when research is fetus-regarding, the pregnant parent might take note that they are the only named participant and mistakenly believe that their health outcomes are central to the research project. I have proposed a co-participants model in which both pregnant parent and fetus are recognized as individual but linked participants under the TCPS2 when relevant to the data analysis types. When a fetus is a participant, proxy consent for their participation is appropriate in many cases, but the pregnant parent is the default SDM and cases where a third party needs to step in will be rare.

My project began by first outlining the reason why this clarity about the status of the fetus is needed. There is currently a call in both literature and guidelines to ensure pregnant people are fairly included in research, but their actual inclusion has been a slow progress. Lucy Langston (2016) suggests that one major reason for this is that REBs default to inaction and not approval when they come across studies that might result in too many risks or harms for fetuses. The problem is, by doing so, no progress can be made for fetal research or pregnancy-related research and harms continue in everyday practice.

Authors such as Wild and Biller-Andorno (2016) suggest that clarity about the fetus within research is a key way to improve ethical research practices during pregnancy. This clarity could also reduce hesitancy from REBs to approve research in pregnancy since it allows a clearer view on who is the target of the research, how the risks and benefits are balanced, and, when proxy consent is involved, provides a clear advocate for the fetal participant to protect their individual interests.

After determining that fetuses can be considered participants under the TCPS2 in at least some research involving pregnancy and advocating for a requirement of proxy consent for their

involvement when it is needed to help improve parental informed consent and to protect both parent and fetal wellbeing, I made specific suggestions for changes to the TCPS2 in order to implement this new understanding of fetal status and the co-participants model. The objections I address in this chapter will apply to the general suggestion of including fetuses as participants and are not specific to the TCPS2.

Section 6.1 looks at “the abortion debate” and addresses concerns that elevating the status of the fetus in research could have implications for medical practice that makes abortion immoral, and the objection that this implication is strong and harmful enough to reject the status of the fetus as a participant. Section 6.2 briefly touches on cases of surrogacy where the pregnant person is not a biological or intended custodial parent of the fetus and might not be an adequate SDM in cases of proxy consent. I then go on to address potential for parental disagreement, which can occur both in cases of surrogacy and in more traditional pregnancies. The concerns about disagreement can lead to undesirable implications for consent and also raise objections for some about the status of the fetus. Objections brought forth in both sections 6.1 and 6.2 rely on the arguments that the negative consequences of treating fetuses as participants under the TCPS2 are strong enough to refuse this change.

Section 6.3 focuses on potential implications and complications related to proxy consent when the pregnant parent themselves needs a proxy, such as in cases of pregnant minors. I finally conclude that, although it is important to address these implications rather than leave them as complications for the change in guidelines, they are not enough to outright reject the clear need for including fetuses as participants under the TCPS2 in relevant medical research.

6.1 The Abortion Debate

Many colleagues and friends with whom I have discussed this work over the years of developing the project have asked “what are the implications of participant status on the status of a fetus as a person, or individual with rights, and how does this work affect or apply to the abortion debate?” This is an important question for me to address because my work as a philosopher or ethicist will not be taken in isolation and, as a responsible academic, I should consider the impact that it might have in other areas, intended or not.

My answer to this question, is that the impact of my work on the “abortion debate” as it is known, is minimal at best. First, as we have seen in Chapter 2 with the status of participant or subject in relation to personhood, there is no strong reason to believe that treating fetuses as subjects in clinical research requires that they be considered moral or legal persons. This is supported by Chervenak and McCullough’s (2011) “fetus as a patient” concept which does not rely on any notion of moral personhood or moral status to determine patient status (p. 44). Instead, they suggest that we use the framework of the fetus as a patient to determine which acts are ethically justifiable. When the fetus can be said to be a patient, physicians are ethically required to protect their interests. This regardless of their developmental stage that might be argued to determine whether they are persons (Chervenak & McCullough, 2011, p. 44). Although I do not find their fetus as a patient model robust enough to adopt, their arguments separating personhood from participant status can guide us in developing and supporting the co-participants model.

The TCPS2 refers to all human participants as “persons” whether or not they possess capacity for rationality, which is often seen as a requirement for stronger concepts of

personhood. The TCPS2 does not discuss non-human animals since it is guidelines for humans, but they do not engage in any discussions of personhood that might be linked to group-belonging or moral community considerations. Both with the “fetus as a patient” and the TCPS2, the concept of personhood is left out of the concept of participant.

Secondly, protections can be provided for fetuses in some contexts that do not extend to others, much in the same way we provide protections for non-human animals and the environment in research differently than we do in other practices. For example, there are rules about how I may treat a chicken were it to be a subject in medical research about chicken health that differ from rules on how I may treat a chicken were it my pet, and of course both of these are different from how I may treat a chicken were I a farmer who sells eggs. The relationship I have with the chicken is what determines the type of treatment I provide for it. Perhaps it would be unethical for me to encourage the chicken to breed, or for me to make a fried egg sandwich for breakfast as a researcher, but completely appropriate to do so were I to house chickens in my back yard in a way that adequately promotes their wellbeing, and simply pick up the eggs they happen to lay.

Although many arguments can be made that it would also be unethical for me raise chickens for the purpose of selling eggs, these arguments are not founded on the basis of particular research contexts, but on an overall argument about what is ethical and unethical for someone to do with chickens in general. If we extend this same reasoning to the treatment of a fetus, it is possible to have different actions in research and practice that are considered appropriate to fulfill the needed obligation towards the fetus and any arguments that are to be made about overarching ethics related to the treatment of fetuses cannot be founded on

particular status within research.

Finally, and perhaps most importantly, even if we can determine the status of a fetus as a person or moral being, that should not be the defining factor when determining the ethics of abortion and its regulation. One may easily respond to my chicken example by pointing out that chickens are not subjects in need of proxy consent in research, so clearly there is something that makes human fetuses different than non-human animals in this regard and that difference is enough to push the status of a fetus into a realm of protection in all potential parts of their life, not just research. However, since we have seen with Mackenzie (1992), Harman (2000), and McCullough and Chervenak (1994) that the obligation to protect fetal interests begins when the pregnant parent commits to using their body for the growth of the fetus, this can easily be applied in non-research contexts as well.

Turning back to the argument that even if fetuses were full moral persons we would not need to outright ban termination as essential health care, we can first look at the arguments from Judith Jarvis Thomson (1971) and see that there is already literature supporting the claim that it is unreasonable for a person to be morally required to give up their entire body, mental and physical wellbeing, to save the life of another. Although Thomson would disagree, some might find successful arguments that one is morally required, or morally responsible to occasionally donate blood, time, or money to save the life of another, but these arguments would not infringe upon the individual's autonomy and wellbeing in the same way. Since arguments supporting the claim that one is not required to give up their autonomy to save the life of another are already a part of the "abortion debate," my work adds nothing new to the discussion that could not be encompassed by the multitudes of those working within ethics of

medical practice have not already considered.

The argument from Thomson is as follows: It is flawed to say that all embryos and fetuses at all stages of development are akin to fully-grown people. This would be like saying an acorn is also an oak tree (Thomson, 1971, 47). However, deciding where to draw the line on the continuum between implanted embryo and full-term fetus is difficult, and that line is very likely to occur before birth. So, by calling all fetuses non-persons we have no way to counter forced-birth arguments, and it is best to grant the claim that all fetuses are persons. The common claim is that fetuses are persons who have a right to life and that right to life outweighs the pregnant parent's right to bodily autonomy. This is where the real work can and needs to be done (Thomson, 1971, p. 48).

After this, Thomson introduces her famous violinist example, which can be summarized as follows: Overnight, the "Society of Music Lovers" has quietly kidnapped you and merged your circulatory system with that of a famous violinist who is in need of your blood to cure his fatal kidney ailment. If you unhook yourself, he will surely die, but the medical treatment takes nine months to complete (Thomson, 1971, pp. 48-49). Thomson takes the position that it would of course be the kind and good thing to stay hooked up to the violinist to save his life, but that in this situation it would be clearly "outrageous" to argue that you have the moral obligation to remain attached to the violinist for nine whole months and that his right to life does not, in fact, outweigh your bodily autonomy in a scenario like this.

She goes on to address the immediate objection one might have that this example is best applied to cases of rape and, therefore, cannot address all issues of pregnancy. Thomson says that, in order to make the argument that abortion is morally accepted in cases of rape, but not

in others, because of the fetuses' right to life, one would have to concede that beings who are a product of rape have low or no right to life in comparison to others and this does not seem like a defensible position (Thomson, 1971, p. 49). I would add that this is especially true if we think a right to life outweighs one's bodily autonomy, which is the main violation that occurs during sexual assaults, and, therefore, clearly something that is of concern to people who want to make exceptions for these cases.

A large part of Thomson's argument hinges on the distinction between rights that are and are not duty-based. A duty-based right is one that comes with it the duty for others to provide the necessities to fulfill your rights. Thomson argues that one's right to life is not duty-based, so, although it is the responsibility of others to ensure they do not kill you, it is not the responsibility of others to ensure you have all the means to stay alive. Forced-birth arguments frame abortions as solely being about the active killing of a human life, but they fail to consider that a fetus' life cannot continue without taking resources from the pregnant parent, resources they have no duty to provide (Thomson, 1971, p. 55). This is on top of the issue of the fetus infringing upon the pregnant parent's bodily autonomy. Thomson then goes on to argue that, even if the death of the violinist is a consequence of unplugging yourself from him, this is not a violation of his right to life because you have not taken from him anything that you owed to him, despite, in a way, taking his life (Thomson, 1971, p. 57).

Finally, Thomson takes a legal approach to point out that nowhere in the world is someone legally required to provide for another being as much as a pregnant person is required to provide for a fetus when abortion is prohibited. In fact, in the United States, you are not even legally required to be minimally decent to prevent someone else's death, let alone give up your

bodily autonomy to keep them alive for nine months, in any case other than pregnancy (Thomson, 1971, p. 63). For example, the Tenth Pennsylvania court specifically ruled that there is no obligation to donate bone marrow to someone in need, even if that person would die without the donation, because it was an “intrusion of the body,” and across the United States, organ donation after death requires consent from the next-of-kin (Manninen, 2010, p. 39).

This line of argumentation is not just seen in Thomson’s work, but also appears in more recent literature around the legality of abortion care in the United States where Bertha Alvarez Manninen (2010) makes the claim that “no one is morally required (and cannot be legally compelled) to submit to unwanted bodily intrusion in order to render aid to another person, even for life itself” (p. 36). This grants the possibility of a fetus being a moral person whose interests should be accounted for while maintaining the position that none of these interests are morally nor legally strong enough to compel someone to remain pregnant against their own desires.

All this is to say that, if we take my suggestion to declare fetuses as participants of human research under the TCPS2, this change in their research status still leaves room for the continuation of the “abortion debate” since 1) this does not necessitate that the fetus is a person and 2) even if the fetus were a person, there are strong arguments showing that abortion is still not an immoral act. Even if the fetus is a full person with basic human rights, those rights do not include the use of another human’s body.

In addition to the concern for the real impact that this change of status might have on medical practice, it is also important to note that calling fetuses participants could have the

unwanted effect of causing prospective participants to believe that their fetus is being given moral personhood status and that, if they enter the study, they will be unable to withdraw consent or seek an abortion. Chervenak and McCullough (2002) address this concern by suggesting that the consent process include clear indications to the pregnant parent that they are under no obligation to enroll or stay in the study for the sake of the fetus, and that they may withdraw consent at any time and seek an abortion if this is their wish (pp. 12-13). I have adopted this suggestion into the co-participants model and would advise that all researchers ensure this is communicated to prospective pregnant participants regardless of whether their fetus is considered a participant.

Why the TCPS2?

Since the focus of my argument is Canada and the TCPS2, I would like to note that currently in Canada there is no specific law restricting abortion at any given point in a pregnancy. So long as a medical professional can perform the procedure safely, it is legal. This is possible in part because not only are fetuses not considered persons, they also are not considered humans for the purposes of things like human rights. Since the TCPS2 is about research on humans, including fetuses as participants under this definition means elevating their status to humans, at least in research purposes.

As I have addressed before, there is no necessary inconsistency with treating fetuses as human participants in research and also allowing abortions in medical practice since the scope of conduct is different in the two different scenarios. However, one might argue that this is a problem for changing the definition of who counts as human in research and could require the

TCPS2 to begin to consider other beings as humans as well and it is best if a new set of research guidelines took this over instead. The obvious first response to this is that fetuses are human and are currently governed by the TCPS2 in regards to research at least as types of “human biological material” even if they are not yet considered participants.

There is no reason to fear expanding the definition of human in research in this way. There is also no reason to fear that this expansion will lead to considering zygotes or gametes human participants because the leading factor concerning the change for fetal status in research is that the development and wellbeing of the fetus as an individual is a central part to research questions during pregnancy. This is not the case for gametes which are aptly placed in the category of human biological material for these purposes. This means that the TCPS2 is in the best position to govern the involvement of fetuses in research, which we have seen in Chapters 4 and 5. Their adherence to commonly held ethical theories and their current rules about protecting fetal wellbeing means there is room to change and expand the guidelines within the TCPS2 to include fetuses as participants without running into significant challenges or inconsistencies.

6.2 Surrogacy and Parental Disagreement

The second implication I will address is the possibility of parental disagreement for fetal participation. First, I will look at cases of surrogacy where the pregnant parent will not become a custodial parent after birth, and second, I will look at disagreement between the prospective custodial parents when one is pregnant. Considering the likelihood that fetuses are subjects in at least some types of clinical research, and that this status as subject (or participant under the

TCPS2) causes the recommendation of proxy consent for their involvement, a serious question is then raised about proxy consent in the case of surrogacy.

For the typical case of a surrogate pregnancy, the pregnant person is the gestational parent and is in an agreement to not be the legal guardian of the child once they are born. This can be the case whether or not the pregnant person is a biological parent of the fetus. From a legal standpoint in Canada, the gestational parent has full rights and control over decisions made about the fetus during gestation, which would extend to cases of research (Reilly, 2007, p. 484). This means the legal guidelines in Canada, if they were to include a need for proxy consent for the fetus, would only require consent from the gestational parent. However, this is not necessarily true for all legislative jurisdictions, and this does not prevent conflicts from arising.

In the example case of *Eye Drops* where the fetus is not a subject or participant of the research because their wellbeing is not part of the research question and their condition will not be recorded by the researchers, there is no reason for the prospective custodial parents to be allowed to influence the consent, or lack thereof, of the pregnant parent Annie to participate in the research. Even outside of Canada where prospective custodial parents, perhaps due in part to their biological connection to the fetus, may have rights pertaining to the actions of the surrogate parent, these rights should not be applied when there is no need for proxy consent of the fetus to participate in research.

For the cases of *Insulin* and *HIV*, these examples involve the pregnant parent having pre-existing health conditions that could affect the health and wellbeing of a fetus and the eventual child, and due to this, people with these conditions are unlikely to enter into surrogate

pregnancy relationships, so I will not be examining the possibility of surrogate disagreement here. However, I will use *HIV* as an example for partner disagreement later on.

With the case of *NIPT*, however, this is a relatively common procedure offered to all pregnant parents in Canada and is an extension of standard screening practices, regardless of any potential health concerns. In this case, if Carson were to be a surrogate parent, legally in Canada they would automatically serve as SDM for the fetus. I have also recommended that in this case that proxy consent should not be used for consent to the fetus' involvement. However, one might argue that were Carson to be asked for proxy consent, they have a moral obligation in this case to defer the role of SDM to a prospective custodial parent. If this is true, it can still be appropriate for guidelines and researchers to merely seek out Carson's proxy consent for the fetus with the understanding that it is Carson's own responsibility to consult with the prospective custodial parents.

If we take a step back, most research during pregnancy does not even require that a researcher know how the prospective participant became pregnant in the first place. For *NIPT*, it could be argued that genetic screening would require a disclosure of something like *IVF* or surrogacy, especially if the pregnant parent is not the egg donor for the fetus, but in most other cases, the research can be conducted without needing to be aware of postnatal legal guardianship agreements. From perspective of research guidelines and REBs, the sole focus should be on the researcher's duties. The duties of the researcher would require that, when gaining proxy consent is recommended for fetal participants, the pregnant parent is an adequate SDM, and no other adults' consent or permission should be sought by the researcher unless there is reason to believe the pregnant parent themselves does not have capacity to provide

their own consent for involvement.

Since the prospective custodial parents have already shown they trust Carson to communicate with them and consider their desires when it comes to the surrogate pregnancy, there is no reason why research cannot also fall under this scope. It is possible that Carson has a surrogacy agreement with the prospective custodial parents to not enter into clinical research without first consulting them, but the contractual duties that Carson has to the prospective custodial parents do not translate into ethical duties of the researcher, nor is the contract meant to limit Carson's participation in research, it is intended to apply to how Carson is allowed to treat the fetus. It is not up to the researchers, nor the TCPS2 to ensure that Carson is fulfilling a possible duty they have to the other parents to be involved in the consent process. The responsibility of discussing the possibilities of research participation during pregnancy is something that Carson and the intended parents would likely need to have before agreeing to enter into a surrogate relationship and potentially be written into the surrogacy agreement before pregnancy takes place. Carson is still an appropriate SDM for fetal consent for the purposes of research and it is up to Carson themselves to ensure they are fulfilling this role adequately while respecting their surrogacy agreement.

Despite the pregnant parent's consent being adequate proxy consent for their fetus, and any other parent's consent not needing to be sought, there still is room for cases of parental disagreement, opening the potential need for adjudication when this disagreement occurs. This is possible both in cases of surrogacy and typical cases of pregnancy. If we call fetuses participants of research and require their proxy consent, one could argue that we are opening up the possibility of a non-gestational parent being able to override the consent of fully grown

adult attempting to join a research study.

To illustrate this example, let us return to *HIV* where Deena is being asked to participate in research testing the efficacy of medication to prevent the transmission of HIV from her to her fetus. This study will begin during pregnancy and requires Deena to take an oral medication up until she gives birth, an intravenous medication during labour, and to refrain from breastfeeding while giving her born child an oral medication for at least six months.

Let us assume that Deena is very interested in this study and, after adequate discussion with a researcher and deliberation on her own, she chooses to sign the consent form for herself and her fetus. However, when she arrives to the clinic for her first appointment to participate, she brings along her partner and the biological father of her fetus, Darren, who has reservations about the study. Darren asks questions of the researcher and decides that he does not want Deena to take the medication because of the potential risks to the fetus. Deena has already consented for her own participation and is an adequate proxy for her fetus, but Darren is so adamant about Deena not taking the medication that the researchers have concerns about whether they have genuine consent for the fetus to participate. This is especially of concern since Darren's dissent might need to be considered once the child is born.

Although it is a fair concern for the researchers to value Darren's objection to the fetus' participation, if Deena were not pregnant and merely brought Darren along as a support person for a trial involving medication for her HIV, Darren's objections would not have any effect on Deena's genuine consent, since Deena is an autonomous adult and does not need Darren's permission to participate in research. In that case, the appropriate action of the researchers would be to kindly suggest to Deena that she bring along a support person who will respect

whichever decision she chooses to make. This is true even when Deena is pregnant, because if we were to take Darren's objections seriously, we would be claiming that Deena needs Darren's permission to participate in this research simply because he is the one who made her pregnant.

Again, the researcher's duties merely include ensuring that Deena has capacity to provide consent for herself, and that they have her genuine consent. This extends to their duty to secure consent for the fetus. Since Deena is an adequate SDM for the fetus, currently the only guardian of the fetus, and the fetus' co-participant in this study, the researchers can fulfill their duties by ensuring that they have voluntary, informed, and ongoing consent from Deena for both her involvement and her fetus. The researchers do not have a duty to Darren since he is not a prospective participant in the study, nor is he a necessary or appropriate SDM for the fetus. This also applies in cases where the other biological parent is not present or known.

This is not to say that Darren's dissent has no moral weight. Since Deena and Darren are in a trusting romantic relationship and have made a commitment to each other to raise the child together once they are born, it can be argued that Deena has a moral responsibility to honour her commitment to Darren. However, this is Deena's responsibility alone. The commitment Deena makes to Darren could be judged as morally binding and we might argue that Deena is acting immorally towards Darren by not consulting him or considering his opinion, but this moral judgement is not part of the researcher, REB, or policy maker's duties or responsibilities.

It is up to Deena to request and consider Darren's opinions on the participation as she sees fit. When Deena signs the consent forms, the researchers must assume that she has fulfilled her commitments to her partner adequately regardless of whether she is pregnant or not. The only

way in which Darren could override Deena's consent appropriately would be if he believed she was not cognitively capable of providing consent for the research. This would, of course, do more than override Deena's proxy consent for the fetus, but also her own consent for her participation if Darren's concerns are substantiated. Section 6.3 will address concerns related to proxy consent for pregnant people who might not have capacity to consent for themselves.

6.3 Minors, Autonomy, and Pregnancy

One complication that could arise for research is when the pregnant parent themselves does not have capacity to consent for various reasons. Some minors are fertile before they are cognitively capable for consent processes and might become pregnant during this time. Adults who have diminished capacity due to cognitive disabilities could also become pregnant, and pregnant people could become incapacitated and incapable of providing consent. In these instances, if the fetus' participation requires consent, then the question arises of how the appropriate SDMs should be chosen and if one person can serve the role of decision maker for both parent and fetus.

It is important to note that capacity for consent is not a clear-cut topic, especially for children. As argued by Turnham and colleagues (2020), in cases of medical practice, it is not appropriate to deny a minor the ability to provide or refuse consent for their born child when they would otherwise be considered capable of making parental decisions about their child (Turnham et al., 2020, p. 359). The argument they make is that minor parents who fulfill the duties of parenthood have demonstrated the same ability as adult parents to provide what's in the best interest of their children within the "zone of parental discretion" (Turnham et al., 2020,

p. 357). This means that, so long as the minor does not require significant assistance in caring for their own child, there is no reason to believe that they are incapable of refusing medical treatment that they find inappropriate for their child's best interests (Turnham et al., 2020, p. 358).

Turnham and colleague's argument was made in the context of refusal of medical treatment for a born child, but the framework could be applied to our case. Although it will be difficult to assess during pregnancy whether a minor is capable of providing the duties of parenthood to their child once they are born, it is important not to dismiss pregnant minors as lacking capacity for appropriate decision making. Some minors can be mature and capable of making decisions for themselves and their overall pregnancy and, if this is the case, there is no need to require a SDM by default for them or their fetus for the purposes of research, regardless of their age. Furthermore, this reasoning could be extended to adults who might otherwise be considered to lack capacity in medical decisions. If they are capable of fulfilling the duties of parenthood, they should not be considered incapable of making medical decisions during pregnancy. This is not to say that an SDM is never appropriate in these cases, but is meant to push back on the automatic assumption that minors are unable to provide adequate consent for themselves and their fetuses or children.

However, there will also be cases where a pregnant minor or adult does lack capacity for parental and medical decision-making. Although it is unlikely for these cases to arise in the research context, the question of an appropriate SDM is warranted. An appropriate SDM for a pregnant parent can follow the same steps as an appropriate SDM for a non-pregnant adult or child. This means someone who is capable of fulfilling the duties of protecting the pregnant

parent's best interests and ensuring their prior wishes, values, or ability to be involved is respected. Both researcher and SDM should ensure they have the pregnant parent's assent when possible and any development of their capacity to provide consent should be accounted for as the research progresses.

Would it be appropriate for one decision maker to serve as a proxy decision maker for both parent and fetus in these cases? I think the simple answer here is yes. Some might argue that the interests of the pregnant parent and the fetus are sometimes in conflict when it comes to health and research and so there could be a formal conflict of interest for the SDM if they have to advocate for both beings. However, we would not find that the pregnant parent is an inappropriate SDM for their fetus due to this conflict, so there is no *prima facie* reason to prevent a single decision maker from fulfilling both roles in the same way a parent with capacity would do.

One concern about the SDM playing a dual role might be that an SDM for a pregnant minor is likely going to be that child's parent and, there is good reason to believe that the SDM parent will value the wellbeing of their child over that of their unborn grandchild, whereas the pregnant parent will value the wellbeing of their fetus more than anyone else. Firstly, it is important to note that a suitable SDM will need to consider the wishes of the person in question as part of their decision making. In other words, if the minor has expressed an interest in continuing the pregnancy and participating in research that could answer questions about the health and wellbeing of the fetus, then it is the SDM's duty to consider these wishes before deciding whether to provide proxy consent on behalf of the minor.

Secondly, the particular circumstance of being pregnant while not having full cognitive

capacity to care for yourself, let alone a born child, places the needs of both pregnant parent and fetus in different contexts than research involving pregnant people who are capable of providing their own consent. This means that, if there appears to be a higher value from the SDM for the safety of the pregnant parent over that of their fetus in these cases, this does not necessarily indicate a bias in favour of the pregnant parent, but rather might indicate a serious consideration of the context and the risks it places on both pregnant parent and fetus, especially in cases where the pregnant parent is a minor and pregnancy poses a larger risk to their health. Beyond the decision making done by the SDM here, it is also important to note that, under the TCPS2, research involving groups with diminished capacity – such as pregnant minors – should only be conducted if their involvement is needed to answer a specific research question and the risk to the participants is minimal unless there is “prospect of direct benefits” (Canadian Institutes of Health Research et al., 2022, p. 71), meaning the potentials for SDMs to find the research inappropriate for the pregnant minor is already reduced.

Conclusion

In this chapter, I have addressed some possible implications and objections to my conclusions in Chapters 4 and 5 that fetuses are subjects of research and may require proxy consent for their involvement. As it pertains to the TCPS2, if a fetus were to be considered a “subject” they would automatically be called a participant, regardless of the conceptual distinction between subject and participant that I have laid out in Chapter 2. Although some of the concerns are overlapping, perhaps the most pressing issue of the change of the status of the fetus comes from those who want to know how this will affect access to abortion in Canada. I have

demonstrated in Chapter 2 that one does not need to be a person to be a subject of research, and, therefore, there is no need to declare a fetus a person in order to consider them a participant under the TCPS2. Nor is there a concern with calling the fetus a human participant, despite the fact that this implies they should be awarded rights of humans. This is because pregnancy is an involved physical process that intrudes upon the body of the pregnant person and any right to life that the fetus might have cannot be said to compel an unwilling pregnant person to continue their pregnancy. Therefore, regardless of whether we think calling a fetus a participant means considering them a person or legal human (which is not a necessary step), there is still room to protect abortion healthcare.

Other concerns that might arise when it comes to requiring proxy consent for a fetus are cases of parental disagreement where the pregnant parent consents to participate and research and is willing to provide consent on behalf of their fetus, but another parent does not wish for them to do so. Although these cases might arise and disagreement should be taken into consideration, the ultimate decision maker would be that of the pregnant parent since they are an adequate proxy for the fetus and requiring alternative consent would mean restricting their own autonomy to participate should someone disagree. The onus of considering all parental agreement before consenting to research on behalf of the fetus is on the SDM, and not on the researchers.

Conclusion

As it pertains to the TCPS2, fetuses can and should be considered participants alongside their pregnant parents in at least some research cases involving pregnancy. The co-participants model in which fetuses are awarded participant status but are still fully linked to their pregnant parent is the best model for implementing this way of understanding the status of the fetus. Fetuses are not currently considered participants by the TCPS2, but they still have protection and consideration unlike any other non-participant biological material, placing them in a position of quasi-status where they are the only non-participants whose interests matter in research and are even central to some research questions.

For the last three decades, bioethicists and other academics have argued that the inclusion of pregnant people in clinical research is essential for the health and wellbeing of pregnant people and their fetuses. A lack of adequate research leaves pregnant people in a position of not receiving care, or only being offered care that has been tested outside of pregnancy; potentially putting themselves and their fetuses at risk. The best way to remedy this harm is by increasing research during pregnancy to ensure treatment offered during pregnancy is thoroughly safe.

However, increasing research during pregnancy is not as simple as recruiting pregnant people into studies that were not designed for their involvement. Despite years of urging by bioethicists and ethics guidelines, research during pregnancy lags behind. One major reason for this gap is the undetermined status of the fetus that has researchers and REBs hesitant to believe that they can adequately protect both pregnant parent and fetus from research risks.

Chervenak and McCullough (2011) emphasize that this hesitancy only leads to further harms and potential exploitation for both pregnant parent and fetus in research and suggest a “fetus as a patient” model for clinical research to help adjudicate these differences (p. 41). However, much like Wild, their work cannot capture the necessary components of what it means to be a research participant in order to determine what role the fetus might play.

In Chapter 1, I walked you through the road so far, why we have arrived at this stalemate of requesting more pregnant people in research and never seeing it. By examining the historical exclusions of women in general and pregnant people in particular, it can be seen that there could be residual fears about vulnerability of the pregnant parent or their fetus, and legitimate concerns that current study models and ethics guidelines were made without pregnant people in mind. This makes the unique situation of having two connected beings whose interests might conflict a difficult challenge that we cannot overcome simply.

In Chapter 2, I examined in detail the general case of what it means to be a participant in research and how this differs from other ways to be involved or affected by research such as being a subject, a collaborator, a co-investigator, or simply a support person. I offered three types of data analysis to help us understand which roles someone might play in research whether they be a fully autonomous adult or a non-human animal and briefly looked at how non-clinical research can give us some insight into what these roles might mean for the clinical research context. I concluded that there is a meaningful conceptual difference between the level of intentional involvement of a subject and a participant and this is consistent with how the terms were intended to be implied, even if they are currently used interchangeably by some guidelines.

In Chapter 3, I took my concepts of subject and participant and the three types of data analysis and determined that yes, fetuses can be considered subjects in at least some research contexts. I argued that, since fetuses fit this general view of a conceptual subject, we should be acknowledging this role that fetuses play, rather than seeing them as factors of complication for the pregnant parent. I then examined four example cases that each held differing levels of involvement for the fetus and parent. *Eye Drops* and *Insulin* were parent-regarding studies in which the main research question centered around parental outcomes. In the case of *Eye Drops*, the fetus was minimally involved, but their data was not analyzed for research outcomes, meaning they were not a subject in that case, but in *Insulin* the fetus was measurably involved.

NIPT and *HIV* were both fetus-regarding trials in which case the research questions centered around fetal outcomes. For *NIPT*, the parent was minimally involved, but still a participant of the research since it would be impossible for their data to not be used for research purposes. In the case of *HIV*, the parent was measurably involved and took on a large number of risks for the benefit of their fetus. The varying levels of involvement between the cases helped us map out boundaries for what could be considered fetal subjects in research and make their application to other cases in the future easier to complete.

Chapter 4 then argued that requiring proxy consent for fetal subjects in at least some cases is a helpful tool for ensuring we follow the principles of Respect for Persons, Concern for Welfare, and Justice for both fetuses and their pregnant parents. This is accomplished by improving clarity about the varying roles in research so the pregnant parent's consent can be truly informed, resulting in increased wellbeing for them and their fetuses. Although it is not my recommendation that fetal subjects always require proxy consent, there are likely to be

benefits from the consent process for most fetus-regarding research studies and many parent-regarding studies that have measurable fetal involvement.

In Chapter 5, I suggested several changes to the TCPS2 that could be easily made to incorporate the co-participants model of fetal participation and proxy consent, and still remain true to the core of the TCPS2 values and its current handling of other participants. The biggest change is that fetuses not imminent to termination will be moved from the category of human biological material and into their own category alongside that of human participants. This includes any fetus intended to be brought to term, and any fetus whose parent is not currently seeking termination. Fetuses imminent to termination, deceased fetuses, or fetal tissue can all remain in the category of human biological material and will be covered under current TCPS2 guidelines. To account for this change, I suggested some wording changes to different sections that will now need to mention fetuses not imminent to termination.

Finally, Chapter 6 addressed potential objections or perceived implications about my work. First, and most importantly, recognizing fetuses as human participants of research does not mean that termination healthcare should be limited. The status of a participant under the TCPS2 is not dependent on any independent moral status such as personhood. Furthermore, even if one could separately make the argument that fetuses have moral personhood or some claim to rights, there are many authors who have argued that these rights are still not enough to trump the right to bodily autonomy of the pregnant parent. Protecting fetal interests and viewing fetuses as future children is done only because the pregnant parent has already agreed to allow the use of their body for fetal growth.

I also addressed in Chapter 6 the potential for issues surrounding consent such as cases of surrogacy or parental disagreement and concluded that any disagreement about the enrollment of the fetus in clinical research is not the researchers' responsibility to adjudicate. The pregnant parent is the most, and often only, appropriate SDM for the fetus and it is important that researchers recognize this when obtaining consent for participation for the parent and their fetus.

For three decades, the inclusion of pregnant people in research has been urged but rarely implemented. Researchers and REBs have been stuck on what it means to be a participant in research and how this pertains to a fetus. With these questions unanswered, the default has been to continue to exclude pregnant people or avoid research surrounding pregnancy. Not anymore. With my co-participants model and the understanding that fetuses should be considered participants under the TCPS2, we have the ability to ensure that pregnant people are included in safe, effective, and ethical research that properly considers the role both they and their fetuses play.

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Appendix A: Policy Changes

Quoted from the TCPS 2 (2022)	Recommended Change
<p>The following requires ethics review and approval by an REB before the research commences. Research involving:</p> <p>a. living human participants;</p> <p>b. human biological materials, as well as human embryos, fetuses, fetal tissue, reproductive materials, and stem cells. This applies to materials derived from living and deceased individuals.</p>	<p>Article 2.1</p> <p>The following requires ethics review and approval by an REB before the research commences. Research involving:</p> <p>a. living human participants</p> <p>b. fetuses not imminent to termination;</p> <p>c. human biological materials, as well as human embryos, deceased fetuses, fetal tissue, reproductive materials, and stem cells. This applies to materials derived from living and deceased individuals.</p>
<p>For the purposes of this Policy, “human participants” (referred to as “participants”) are those individuals whose data, biological materials, or responses to interventions, stimuli or questions by the researcher, are relevant to answering the research question(s). (p. 14)</p>	<p>For the purposes of this Policy, “human participants” (referred to as “participants”) are those individuals whose data, biological materials, or responses to interventions, stimuli or questions by the researcher, are relevant to answering the research question(s). “Fetuses not imminent to termination” includes any gestating fetus whose pregnant parent is not currently seeking termination, and whose data or interests are relevant for research outcomes. For example, a study seeking to determine the effects of insulin regimens on gestational growth.</p>

<p>In some cases, research may involve interaction with individuals who are not themselves the focus of the research, in order to obtain information. For example, one may collect information from authorized personnel to release information or data in the ordinary course of their employment about organizations, policies, procedures, professional practices or statistical reports. Such individuals are not considered participants for the purposes of this Policy. This is distinct from situations where individuals are considered participants because they are themselves the focus of the research. For example, individuals who are asked for their personal opinions about organizations, or who are observed in their work setting for the purposes of research, are considered participants. (p. 16)</p>	<p>In some cases, research may involve interaction with individuals who are not themselves the focus of the research, in order to obtain information. For example, one may collect information from authorized personnel to release information or data in the ordinary course of their employment about organizations, policies, procedures, professional practices or statistical reports. Such individuals are not considered participants for the purposes of this Policy. This includes fetuses where research questions and outcomes are focused on the pregnant individual and do not involve monitoring fetal outcomes.</p> <p>This is distinct from situations where individuals are considered participants because they are themselves the focus of the research. For example, individuals who are asked for their personal opinions about organizations, or who are observed in their work setting for the purposes of research, are considered participants.</p>
<p>For the purposes of this Policy, human biological materials include tissues, organs, blood, plasma, serum, DNA, RNA, proteins, cells, skin, hair, nail clippings, urine, saliva, and other body fluids. Materials related to human reproduction include embryos, fetuses, fetal</p>	<p>For the purposes of this Policy, human biological materials include tissues, organs, blood, plasma, serum, DNA, RNA, proteins, cells, skin, hair, nail clippings, urine, saliva, and other body fluids. Materials related to human</p>

<p>tissues, and human reproductive materials. (p. 16)</p>	<p>reproduction include embryos, deceased fetuses, fetal tissues, and human reproductive materials.</p>
<p>Article 4.3</p> <p>Women shall not be inappropriately excluded from research solely on the basis of their reproductive capacity, or because they are pregnant or breastfeeding.</p> <p>Application</p> <p>Researchers should not exclude women from research on the basis of their capacity, or their pregnancy, or because they are breastfeeding, unless there is a valid reason for doing so.</p> <p>Subjecting women of childbearing potential to inappropriate requirements precludes their participation in research. Exclusions should be made on the basis of clear criteria that reflect attention to the potential benefits as well as the foreseeable risks of the research that may affect the welfare of women. For example, researchers should not require participants to use oral contraception, unless there is a valid reason for doing so.</p>	<p>Article 4.3</p> <p>Women shall not be inappropriately excluded from research solely on the basis of their reproductive capacity, or because they are pregnant or breastfeeding.</p> <p>Application</p> <p>Researchers should not exclude women from research on the basis of their capacity, or their pregnancy, or because they are breastfeeding, unless there is a valid reason for doing so. This policy also extends to people of other genders who have similar child-bearing capacities.</p> <p>Subjecting women of childbearing potential to inappropriate requirements precludes their participation in research. Exclusions should be made on the basis of clear criteria that reflect attention to the potential benefits as well as the foreseeable risks of the research that may affect the welfare of women. For example, researchers should not require participants to use oral</p>

<p>In considering research on pregnant or breastfeeding women, researchers and REBs shall take into account foreseeable risks and potential benefits for the woman and her embryo, fetus or infant, as well as the foreseeable risks and potential benefits of excluding pregnant or breastfeeding women from the research.</p>	<p>contraception, unless there is a valid reason for doing so.</p> <p>In considering research on pregnant or breastfeeding women, researchers and REBs shall take into account foreseeable risks and potential benefits for the woman and her embryo, fetus or infant, whether the fetus is a participant in the research project, as well as the foreseeable risks and potential benefits of excluding fetuses and pregnant or breastfeeding women from the research.</p>
<p>N/A</p>	<p>Research Involving Fetuses Not Imminent to Termination</p> <p>The core principles of Justice and Concern for Welfare entail special ethical obligations toward fetuses not imminent to termination. This section sets out conditions that apply to research involving fetuses intended to be brought to term or where their parents are not actively seeking termination.</p> <p>Article 4.7</p> <p>Subject to applicable legal requirements, fetuses not imminent to termination shall not be inappropriately excluded from research. Where a researcher seeks to involve fetuses not imminent</p>

	<p>to termination, the researcher shall, in addition to fulfilling the conditions in Articles 4.3 and 12.6 where appropriate, satisfy the REB that:</p> <ul style="list-style-type: none">a. The research question can be addressed only with fetal participants and their co-participant parent; andb. The research does not expose the fetal participants to more than minimal risk without the prospect of direct benefits for them. <p>Application</p> <p>Fetuses lack the capacity to decide whether to participate in particular research initiatives. As a result, they have, historically, experienced hesitancy and unjustified exclusion from research. Yet the advancement of knowledge about their health experiences and needs may depend on their appropriate participation in research. Their inclusion in research requires special considerations as outlined in this article and article 4.3 for their co-participant parent.</p> <p>To be ethically acceptable, the participation of fetuses and their co-participant parents shall be necessary and appropriate to address the research question. Researchers and REBs shall consider the level of risk to which fetal participants are exposed, and the prospect of direct benefits</p>
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	<p>accruing to both co-participants. Fetal participation should generally be limited to research of minimal risk as defined in this Policy. See Chapter 2 for the definition of minimal risk.</p> <p>The research design shall take into account the effects of the intervention on fetus and parent and clearly indicate if fetal outcomes or parent outcomes are central to the research question. The proxy consent needed for fetal participation shall default be awarded to the co-participant parent unless they lack decision-making capacity. No third-party consent beyond the co-participant parent is needed for fetal participation.</p> <p>For research involving pregnant people where fetuses are not involved at the level of co-participants, including when fetal tissue is being used, refer to articles 12.6 and 4.3.</p>
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