Informed Consent in the Context of Vaccination

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EXECUTIVE SUMMARY

Improving the health literacy of patients in relation to medical practices and research is essential for upholding the principle of respect for autonomy - that is, respecting the patient’s ability to make self-governed choices regarding medical interventions or research participation that reflect the patient’s beliefs and values. This report provides a review of informed consent challenges (i.e. ethical gaps, barriers, and priority needs) that are unique to certain vulnerable groups, namely preadolescents, adolescents, and pregnant women, with a specific emphasis on three vaccination cases: the meningitis, Respiratory Syncytial Virus (RSV), and Human Papilloma Virus (HPV) vaccines. The objective is to offer recommendations on how these gaps, barriers, and challenges may be solved or avoided in the future. The challenges can be categorized into two. The first is comprised of challenges that are patient-centered, which prevent a research subject from fully understanding the disclosed information. The second is comprised of challenges that are process-centered, which are procedural barriers that prevent practitioners from truly obtaining informed consent from prospective patients.

The types of recommendations explored in this report for solving or avoiding consent barriers in the context of vaccine administration and research include: 1) improving the readability and design of consent forms, 2) incorporating education-specific strategies to improve patients’ or participants’ understanding of consent information, 3) initiating discussion of meningitis, HPV, or RSV immunization and clearly explaining the benefits of infection prevention through immunization, 4) inviting questions at every step of the consent process, 5) acknowledging and addressing discrimination based on age and gender, 6) obtaining consent from legal representatives (in the case of children, adolescents, and pregnant women limited by mental defects or disorders), 7) protecting the privacy of participants enrolled in vaccine-related research, 8) acknowledging the experiences of patients or participants with meningitis, RSV, and/or HPV infection, 9) implementing procedures to assess the capacity of patients or participants to consent, 10) supporting parenting strategies and lifestyle practices that reduce and reverse predisposing risk factors to meningitis, RSV, and HPV infection, 11) adopting individualized approaches to promote health protective behaviours by tailoring the consent process to reduce concerns relating to vaccine cost, pain, safety, side effects, perceived appropriateness to lifestyle, and/or need for multiple doses, and 12) implementing a dynamic informed consent model with participant control, accompanied by appropriate privacy safeguards.
INTRODUCTION

This report will identify the ethical gaps, barriers and challenges currently present in obtaining informed consent in two contexts (i) prior to the administration of vaccines, and (ii) during transitional/clinical vaccine research involving human participants. It will also identify the priority needs that arise under these two contexts that apply specifically to vulnerable populations (i.e. young people and pregnant women), by discussing three vaccination cases (i.e. the novel meningitis vaccines, the Respiratory Syncytial Virus (RSV), and the Human Papilloma Virus (HPV)).

This report is divided into three parts. Firstly, the report will discuss the universal principles regarding informed consent in general, and which are applicable both prior to the administration of vaccines, and during transitional/clinical vaccine research involving human participants. Secondly, the report will identify additional ethical gaps, barriers and challenges present when considering specific vulnerable populations, namely preadolescents, adolescents, and pregnant women, in the particular cases of the novel meningitis vaccines, the Respiratory Syncytial Virus (RSV), and the Human Papilloma Virus (HPV). By identifying the ethical gaps, barriers and challenges that apply to these vulnerable populations in these particular vaccination cases, this report will be able to highlight some specific principles of informed consent to safeguard the priority and needs of said populations. Based on the principles identified in parts one and two, the report will then present in part three some recommendations for obtaining informed consent for vaccination. These recommendations will highlight the priority needs that should be addressed in the context of informed consent for the administration of vaccines and for the transitional/clinical vaccine research in general, with an emphasis on vaccination cases involving young people and pregnant women.

1 Undue influence is a legal doctrine that involves one person taking advantage of a position of power over another person to exert his or her authority.
overall public will impact an individual’s risk of infection (4). In one study the researchers used a computerized experimental game in order to simulate a hypothetical disease. The results of the study indicated that each participant’s vaccination decision depended on the vaccination decisions of other participants (4). Throughout the study it was revealed that the free-riding behaviour was present regardless of whether the hypothetical disease was severe or mild, whether the risk of infection and the cost of vaccination was high or low, and whether the participant played as an elderly or young person (4)."

Although the decision to get vaccinated should be free from any undue influence, the above analysis shows that vaccination policies can be undermined. As such, in order for vaccination programs to be effective, the free-riding behaviour has to be taken into consideration. This behaviour is a factor that was considered to be highly important when developing the guidelines for informed consent.

B. Informed Consent for Vaccination during transitional/clinical vaccine research involving human participants

According to the Belmont Report, in order to respect the research subjects, two ethical principles must be adhered to. The first principle is that individuals should be treated as autonomous agents. This will enable them to make decisions about their health only after being informed of what they are consenting to, while being free from the control of others. In the context of respecting the first principle of informed consent, vaccination research requires that subjects be informed of all relevant details pertaining to their participation (i.e. project or vaccination objectives, identity of researchers/clinicians, anticipated outcomes, and potential risks and benefits among others) before making a decision as to whether or not to participate (5).

The second principle is that individuals with diminished capacity are entitled to extra protection. In order to adhere to this principle, researchers must obtain consent from the patient, or someone who is legally authorized to provide informed consent on the patient's behalf. This individual is consenting on behalf of the patient only after being fully informed of all the risks and benefits (6).

Based on our preliminary analysis of existing consent challenges (in the context of translational/clinical research in Canada and abroad), this report has identified the possible barriers that researchers face in obtaining informed consent from participants, particularly in regards to the second principle. These fall under two categories: patient-centered and process-centered.

1. Patient-Centered Barriers

For purposes of this report, the patient-centered barriers are useful not only in formulating principles that deal with vaccination research, but also in formulating principles that deal with the administration of vaccines. Patient-centered barriers prevent a research subject from fully comprehending the disclosed information.

Specifically regarding vulnerable groups, patient-centered barriers include: developmental, illness-related and psychological/cultural factors. These will be discussed in further detail later in the report.

2. Process-Centered Barriers

Process-centered barriers are useful in formulating principles that should be followed in translational/clinical vaccine research. Barriers beyond the mere signing of a consent form need to be addressed. These potential barriers include issues around timing. For example, at which point during disease-progression was the informed consent sought? Additionally,

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2 For instance, some diseases may impact the patient's cognitive capacity at certain points of progression.
the length of time provided to patients to fully understand the information distributed by the physician in order to make a decision can also play a factor. Finally, the content and readability of consent forms are also considered to be important barriers that need consideration (6).

Specifically regarding vulnerable groups, process-centered barriers include various factors external to the patient. These will be discussed in further detail later in the report.

There remains a need to identify key principles for overcoming these barriers to informed consent. These principles are recommended to be used as a foundational blueprint for obtaining informed consent in the context of research (3).

II. INFORMED CONSENT FOR VULNERABLE GROUPS: PRIORITY NEEDS AND SPECIFIC PRINCIPLES

To understand the complexity of informed consent associated with vulnerable groups, three specific vaccination case studies will be emphasized: namely, the novel meningitis, Respiratory Syncytial Virus (RSV), and Human Papilloma Virus (HPV) vaccines. This report will highlight how vulnerable groups (specifically preadolescents, adolescents, and pregnant women) require additional considerations beyond the general principles discussed. This section will first discuss a proposed framework when assessing informed consent in these populations. Second, it will apply this framework to these vulnerable groups, with emphasis on each group’s specific needs. Third, the report will propose principles that should be implemented to improve the administration of these three vaccines, meningitis, RSV, and HPV, to members of the vulnerable groups that we focused on.

A. Framework for Additional Ethical Considerations in Dealing with Vulnerable Groups

1. Defining vulnerability

There is a presumption that vulnerable groups are especially susceptible to being unduly influenced into providing consent, and therefore have a rightful claim to special consideration or protection. A group is generally considered to be vulnerable when they have a “compromised ability to protect their interests and provide informed consent (7).” Providing any meaningful ethical guidance to informed consent challenges in this context necessitates defining the essential traits and scope of vulnerable persons or populations (8). More precisely, understanding the concept of vulnerability through multiple lenses is key to understanding the consent challenges in the context of vaccination cases and clinical research.

A common pattern in international declarations and ethical guidelines of defining vulnerability is to focus solely on specific populations, for example women, children or ethnic minorities. This pattern has been criticized as it may lead to the implication that individuals who are members of these populations are inherently vulnerable in all situations (e.g. 3 in particular, where participants’ consent may be required to obtain, use, and share collected, personal health information (i.e. in human tissue or data).

4 In terms of a more context-derived definition of vulnerability, we may seek guidance from the United States (U.S.) federal government, which identifies—via a context-sensitive approach—specific populations given extra protection in the Code of Federal Regulations (CFR)#4: these include pregnant women, human foetuses and neonates#5, prisoners#6, and children#7, among other groups. Although the CFR does not present an exhaustive list of vulnerable populations, what is provided is a concept of vulnerability that is based upon the following factors: ability to consent, risk and reward in the study, potential for coercion, and choice of subjects#8.}

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vulnerability in all cases of vaccination or clinical research) (9). In this regard, the National Bioethics Advisory Commission (NBAC) has argued that “vulnerability is sensitive to context and individuals may be vulnerable in one situation but not in another (10).” In other words, the NBAC has suggested that vulnerability should be defined in terms of context rather than in terms of specific groups. For instance, where gender intersects with poverty, the social vulnerabilities faced by women belonging to this lower socioeconomic group are exacerbated. However, such categorization does not necessarily prove that our target group is vulnerable in all cases of vaccination and clinical research.4

As a procedural solution to accommodate the needs of our target group, the model of informed consent in itself must first be defined. Specifically, meaningful ethical guidance (for informed consent challenges involving children, adolescents, and pregnant women) requires clarification regarding what the “informed” criterion for consent in law and policy substantively entails. Informed consent must be given voluntarily, and this voluntarism can be diminished by factors such as “developmental immaturity, cognitive deficits, illness, and pressures present in certain settings (11).” In such instances, it is important that the consent obtained by the physicians is without undue influence or coercion. Physician coercion refers to the undue influence that a physician can exert on a patient, when the patient is required to make a decision. Power dynamics between physicians and women or racial minorities have also been shown to impact a person’s ability to decide on courses of treatment (11). Thus, to obtain informed consent, appropriate information must be provided while ensuring that the patient is not being unduly coerced.

2. Model of Informed Consent for Vulnerable Groups

When working with vulnerable groups, consent includes four additional considerations. These are: developmental factors, illness-related considerations, psychological and cultural issues, and external pressure (11). These in turn can be related to eight traits of vulnerability identified by the Institutional Review Board for Social and Behavioral Sciences (IRB-SBS) at the University of Virginia.5

a) Developmental Factors
Development in the form of “cognitive ability, emotional maturity, and moral character” all have an impact on the voluntariness of the consent provided (11). Cognition is integral to voluntariness, as patients must understand the significance and the impact of their consent (12). Having the capacity to provide informed consent includes the abilities of “(understanding), logical reasoning, communicating a well-reasoned choice, and appreciating the significance of the decision made (13).” Cognitive or communicative vulnerability thus signifies that the participant is unable to process, understand, appreciate, and reason through the consent documentation and/or explanations due to either mental or language limitations. For example, the developmental capacity of children must be considered, and their ability to make decisions must be differentiated from their ability to make informed decisions regarding their health.

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5 The University of Virginia has identified eight traits of vulnerability that may interfere with an individual’s ability to protect themselves in research or clinical interventions—especially during the informed consent process.
Age and level of education have both been shown to have detrimental impacts on a patient’s comprehension of the informed consent process. In particular, the ability to read is central to the capacity for providing informed consent. Excessive length and complex language reduces the comprehensibility of consent forms (14). Furthermore, a deficiency in mental ability results in patients providing consent without fully understanding the risks associated with their participation (13) (6).

b) Illness-Related Considerations
Mental and physical illnesses are detrimental factors in that they diminish the quality of consent. This includes individuals whose medical state may cloud their ability or judgment to make an informed decision regarding study participation. For instance, a patient may perceive a research study as a miracle cure to their disorder rather than a procedure with no guarantee for results. The presence of the symptoms of an illness may hinder an individual’s ability to ensure that their motivations for providing consent are appropriate (11). However, the presence of a mental disorder in a patient must not be instinctively linked with the incapacity to make an informed decision about a medical treatment. A patient with mental illness is therefore presumed capable of consenting to treatment or research until sufficient evidence points to the contrary (15).

c) Psychological and Cultural/Religious Values
A patient’s cultural disposition and past experiences with medical health care professionals will have an impact on the level of trust that they have in a vaccine’s efficacy. Although local culture may shape people’s perception over time, people are more likely to trust experts that inherently share a similar culture (16). When working with ethnic minority patients, it is important to note that comprehension may also transcend simple linguistic barriers. The conceptualization of illness and cultural bias both play a role in the ways that information is presented and understood. Thus, it is important to understand the role that culture plays in obtaining informed consent (17). In particular, in multi-cultural societies composed of immigrants with varying cultural backgrounds, differing attitudes regarding the role of physicians may exist.

Moreover, the quality of informed consent may be dependent on the relationship between a physician and their patient. To improve the physician-patient relationship, and for the consent gained to be effective, a partnership based on openness, trust, and good communication needs to exist (18). An individual’s religious beliefs or related cultural values can lead to questions and concerns that health professionals, unfamiliar with the particular religion or culture, may not have encountered before. Patient trust as well as a positive open attitude from the health professionals need to mutually exist (7).

It has been shown that culture, which can also include religious and spiritual backgrounds, can impact one’s vulnerability to infectious diseases. Rejecting vaccination due to religious or cultural values is not a new phenomenon: there have been numerous reports of vaccine-preventable outbreaks in religious schools, congregations and religious communities (19). As a case study, the World Health Organization reported that only 16% of the children in a region in Nigeria were

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6 In addition, the presence of any preexisting illness may risk exposing associated psychological problems that would impact a patient’s autonomy and their ability to provide informed consent.

7 This factor is also important in the light of the “free-rider” behaviour that has been previously discussed in this report. Should the implementation of vaccination programs be a potential problem in specific populations composed of immigrants, countries will have to be mindful of an individual’s cultural dispositions in order to avoid the loss of a vaccine’s efficacy through the free-rider mentality.

8 For instance in 1853, in order to oppose the compulsory vaccination act, people in the United Kingdom formed the Anti-Vaccination League (20).
<table>
<thead>
<tr>
<th>Religion</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Judaism</strong></td>
<td>Believers are allowed to take certain proactive measures to maintain their health.</td>
</tr>
<tr>
<td></td>
<td>Community health is regarded highly; there is a duty to protect one's children and neighbours from harm.</td>
</tr>
<tr>
<td></td>
<td>Some dietary restrictions on medication exist; in particular, the kosher limitations may apply to oral administration of some drugs, but not to injections. Even then, authorities still consider the importance of preserving life.</td>
</tr>
<tr>
<td><strong>Christianity</strong></td>
<td>There are various Christian denominations where most have no objections to the use of vaccinations.</td>
</tr>
<tr>
<td></td>
<td>According to Grabenstein, denominations with no objection include Roman Catholicism, Eastern Orthodox and Oriental Orthodox Churches, Amish, Anglican, Baptist, the Church of Jesus Christ of Latter-day Saints (LDS), Congregational, Episcopal, Lutheran, Methodist (including African Methodist Episcopal), Pentecostal, Presbyterian, and Seventh-Day Adventist Church.</td>
</tr>
<tr>
<td></td>
<td>Jehovah's Witnesses' authorities have taken a neutral position on vaccination, and they have stated that blood derivatives may be accepted on certain occasions.</td>
</tr>
<tr>
<td></td>
<td>The Roman Catholicism and a few other Christian denominations have expressed some concern to the “aborted fetal origins of the principal formulation of rubella vaccine and some cell lines used to manufacture certain types of viral vaccines”.</td>
</tr>
<tr>
<td><strong>Islam</strong></td>
<td>Many Islamic leaders have issued statements to inform their followers that immunization is in line with the Islamic principles.</td>
</tr>
<tr>
<td></td>
<td>Importance is also placed on the protection of others through vaccines through the rule to protect all lives.</td>
</tr>
<tr>
<td></td>
<td>Dietary concerns can be eliminated for the sake of advancing the health of an individual.</td>
</tr>
</tbody>
</table>

Table 1: Religious views concerning immunization.
vaccinated against polio. The low vaccination rates in this predominantly Muslim community is said to be due to the community-wide belief that the polio drops are used as a tool to sterilize the children. Likewise, a study from the Netherlands has shown that some municipalities with a high orthodox protestant population have lower vaccination rates compared to other municipalities (20).

A discussion of the varying perspectives of specific religions or cultures with regards to vaccination programs is outside the scope of this paper. However, an objective summary of the key teachings of three religions authorities (Judaism, Christianity, and Islam) with respect to immunization is provided. These specific religions and cultures were selected due to their prominence in North America and European Countries.

d) External Factors
There are additional external systemic vulnerabilities that can impact the consent obtained from a patient. The following is a non-exhaustive overview.

Institutional vulnerability is an external factor whereby individuals are formally subordinated to an authority figure and their consent may be coerced either directly or indirectly. Examples include prisoners, student/teacher relationships, or employee/employer relationships.

Deferential vulnerability includes individuals that are informally subordinated to an authority figure and who may feel obligated to follow advice (such as to consent) from such authority. For example, abuse victims, doctor/patient relationships, or husband/wife relationships.

Economic vulnerability includes individuals whose economic situation may make them vulnerable to the prospect of free medical care and/or the payments issued for participating in a study.

Legal vulnerability includes participants that do not have the legal right to consent or those concerned that their consent could put them at risk for legal repercussions (e.g. forfeiture of health insurance coverage due to potential associated risks of genetic discrimination).

Lastly, there is social vulnerability, which includes individuals that are at risk for discrimination based upon race, gender, ethnicity, and/or age. For example, physicians or researchers may not offer a comprehensive explanation in the consent process owing to prejudicial attitudes against women or because they presume that the individual under their care is not able to understand the information due to their young age. Furthermore, the ways in which race plays a role in asymmetrical power relationships between a patient and physician must also be considered (17). Physicians may unintentionally reiterate racial bias into their practice and may also lack cultural competency in understanding the patient’s understanding of illness (21).

The traits most relevant to the target groups discussed and which therefore warrant consideration are: cognitive or communicative; social; and legal vulnerabilities. See Part (c) below for proposals on how specific consent barriers presented by these three vulnerability traits may be solved or avoided.

B. Vaccination Involving Vulnerable Groups: Preadolescents, Adolescents, Pregnant Women, and Their Specific Needs

The informed consent process poses several ethical challenges,
where failure to obtain informed consent may result in the violations of individuals’ human rights. Diverse factors such as poverty, disease, lack of education, hardship and submissiveness, to the effects of war, famine, pandemics, and social insecurity all play a role in making participants and patients more vulnerable to research exploitation. (9) Such factors must therefore be considered by clinicians and researchers alike in their efforts to seek informed consent, especially among vulnerable groups (15).10

Patient-physician communication is integral to “building a therapeutic doctor-patient relationship (22).” Effective communication plays a large role in regulating a patient’s emotions, aiding in well identifying a patient’s perceptions and expectations as well as facilitating their ability to understand medical information (22). The patient-physician relationship must also be understood in the context of historical and social relationships, the latter of which includes race, socioeconomic status, education and gender among others (23).

The patient-physician relationship is at constant odds between the need to provide the physician with the full decision-making power and to provide patients with the autonomy over their treatment decisions. Control must be shared, particularly when working with vulnerable populations, in order to transform the relationship into a partnership (23).

1. Children

Informed consent rests on the notion that a patient comprehends the nature of the treatment and his or her rights with respect to the treatment. In ethics and law, minors are presumed to lack the ability to understand the nature of such decision-making because of lesser developed cognitive functions and power differentials within the patient-physician relationship (24).

The decision-making capacity in children varies depending on the age, circumstances, mental status, and the risks associated with their decision (25). The ability of children to provide consent develops as they mature, and thus developmental factors play a large role in addressing the validity of their informed consent.

It becomes important to differentiate between the cognitive functions and social experiences of the age groups of minors. Preadolescent children should be excluded from providing meaningful consent, whereas adolescents 14-years old and above may participate in decision-making in more concrete ways. In Piaget’s four stages of intellectual development, adolescents are viewed to be equally as cognitively developed as adults (24). As noted by Piaget, at this age, “intelligence is demonstrated through the logical use of symbols to abstract concepts” such as those of their rights. It has been shown that from the ages of 14 and above, adolescents have a marked change in the ability to understand their rights and personal autonomy through self-determination (24). Within this age group, adolescents are able to demonstrate a level of competency equivalent to that of adults based on four standards of competency: evidence of choice, reasonable outcome, rational reasons, and understanding (25).

Prior to this age, children see rights as “arbitrarily granted by adults,” but as they grow older, they understand the concept through a lens of social order (24). It is important to note however that “children as young as nine” are still able to provide preference in their treatment options, despite not fully considering critical components of risks disclosed to them. Thus, both the assent and dissent of pre-adolescent children must be considered when considering the administration of vaccines. Children within this age group should be involved in decision-making processes regarding their health, but not provide a fully autonomous role in decision-making (25).

10 E.g. Lower literacy rates and minority status have both been shown to be determinants of comprehension in providing consent
EXECUTIVE SUMMARY

Generally, decision-making regarding the health care of young patients is a shared responsibility between the physician and the parents or guardians. Thus, parent must provide consent (with the elements of standard informed consent) prior to the administration of medical treatments (26, 27). Particularly, with children, informed consent becomes difficult to attain because it is often given through a proxy – their parents or guardians (14). Where a minor does not have the capacity to consent to an intervention, the intervention may only be carried out with the authorization of his or her representatives or an authority or a person or body provided for by law. This surrogate decision-maker generally acts in the “best interests of the child”, but this principle has proven to be difficult to define. Cultural values regarding child-rearing play a large role in these decisions (26). This creates an ethical dilemma, as those providing consent are often thinking foremost in their roles as caregivers, and not in the child’s best interest.

Children should not be treated as completely rational decision-makers, but should participate in the decision-making process. Information should be provided to pre-adolescent and adolescent children in an age-appropriate manner, which takes into consideration their health literacy (28). Basing voluntariness on the development of the individual children means that this group should be able to make decisions within their capacity; otherwise a legal surrogate should make the decision (25).

2. Women/Gender

Gender has been shown to impact the quality of healthcare (23). Physicians must critically consider the ways in which gender may impact their relationship with patients in order to avoid reinforcing gendered bias. Physicians must be particularly cognizant of the ways in which their decision-making authority acts as a power structure within the construction of gender. Gender and power relations create an asymmetrical relationship, whereby the physician is the “holder of knowledge, authority, activity and dominance” and the female patient is a passive participant (23).

Furthermore, gender plays a role in the variation of communication style between individuals (29). These differences in communication style impact patient communication, as studies have shown that patient behaviour reciprocates gender-linked physician behaviour (29). Studies in feminist critical thought have noted that women often perceive things through an emotional ‘lens’, which in turn makes them more vulnerable as a patient thus requiring additional protections (30). Additionally, gender concordance results in more lengthy visits and equal contributions from both parties regarding medical dialogue (29).

Lastly, gender also plays a role within the context of culture and family relationships. In some communities, women may express their wishes to have a male relative’s permission prior to providing consent for treatment (31).

3. Pregnant Women

Ethical issues also arise in clinical research that involves pregnant women as participants (32). Specifically, ethical issues arise as a consequence of the interdependence between the health of the mother and the fetus. Generally, a pregnant woman is able to protect her own interest (15). However, a pregnant woman is also responsible for protecting the interests of her fetus, which is unable to provide consent (15, 33). A fetus may have unique risks and other health-related issues to be considered by the mother when providing consent (15). One such consideration is the vaccine’s ability to

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11 Studies have shown that parents are less likely to have their children vaccinated if the majority of other children are vaccinated. For instance, as mentioned by O’Neill, parents have been given the right to refuse to have their children vaccinated in the United Kingdom. The proportion of children vaccinated with measles, mumps, and rubella (MMR) has now fallen; free-riders now face a problem of being less likely to be protected despite not being vaccinated.
be protective and safe for both the mother and fetus because of the antibody transfer by the placenta (33). The mother’s decision to protect herself from an infectious disease through vaccination may also pose therapeutic benefits and risks to the fetus (15). Thus, communication with a pregnant woman is incredibly important as any perceived benefits or risks to either her or the fetus may play an important role on decision-making (34).

C. Principles of Informed Consent in the Context of Three Vaccination Case Studies: Meningitis, RSV, and HPV Vaccines

Both unvaccinated and inadequately vaccinated individuals can pose a serious risk to others within their communities due to the potential for transmission (in the community) of infectious diseases. In using vaccines against meningitis, RSV, or HPV—like with all vaccines—the implementation of ethical principles should be balanced with promotion of adequate vaccination. The ethical challenges in the specific context of meningitis, RSV, or HPV vaccination arise from the fact that the main target group for immunization includes vulnerable persons: infants, preadolescents, adolescents, and pregnant women. Clinicians and researchers will therefore inevitably face challenges in satisfying the requirements of customary fully informed consent norms among this target group.

Specifically, to satisfy the requirements of an ethically valid informed consent, each member of this group - including parents as proxies for infants, preadolescents, and adolescents - must be given the opportunity to not only ask questions pertaining to the vaccination, but to also receive appropriate answers to such questions. The following considerations must be disclosed to the vulnerable groups identified: (1) the condition for which the vaccination is proposed, (2) the nature of the proposed interventions (i.e. regimens, doses, and schedules), (3) the risks and benefits that a “reasonable person” would expect to be divulged, and (4) alternative courses of infection prevention (35). Collectively, these considerations require that clinicians and researchers disclose all information that a “reasonable” patient or participant would require in order to reach an informed decision about vaccine administration or research.12

The idea of a “reasonable person”, as alluded to in Canadian case law, needs to take into account that the patient or research participant, especially one that is vulnerable and marginalized in society: (1) is not an expert in the medical field or the study, and (2) relies on the clinician’s or researcher’s “special skill, knowledge and experience,” which puts the clinician/researcher in a fiduciary position (36, 37). This fiduciary position arises from a duty to ensure, at all times, the right of the individual to the safeguard of their integrity, which is an ethical obligation arising from the World Medical Association’s Declaration of Helsinki (38).

1. Consent Barriers: HPV Vaccination

There have been focused efforts through research to identify consent barriers to HPV vaccination; certain elements proposed are highly transferable to the meningitis and RSV vaccinations. To this end, a study examining HPV vaccine promotion in the African-American community has identified the following key factors affecting HPV immunization among African-American mothers and their adolescent daughters (39):

1. Experience: The mothers’ experience of cervical dysplasia and cervical cancer (CD/CC)13 motivated a strong commitment to protect their daughters from the trauma of CD/CC;

2. Comprehension: Limited understanding of HPV and its connection to CD/CC among the mothers made it difficult for them to evaluate the risk of infection or to explain the

12 The patient must understand the information disclosed, and a voluntary decision must be made based on the information presented.
medical benefits of the vaccine to their daughters;

3. Advocacy/Endorsement: The mothers’ anticipation of their adolescent daughters’ sexual activity, leading the mothers to advocate for health care interventions to protect their daughters; and

4. Trust: The mothers’ trust in their physicians to initiate discussion of HPV immunization.

This study also revealed that mothers trusted physicians to initiate discussion of HPV vaccination. Physicians who failed to initiate discussion — and thereby failed to seek informed consent for vaccination — generated doubt about the vaccine among mothers, and consequently, created missed opportunities for immunization among adolescent women.

Additionally, a mix of perceived barriers to HPV vaccination has been identified in a separate study by Florida State University. This investigation concluded that perceived barriers to behaviour change are influential determinants of health behaviour; these include women’s intentions to receive the HPV vaccine. Specifically, vaccine cost, pain, safety, side effects, perceived appropriateness to one’s lifestyle (e.g. not being sexually active), and need for multiple doses, were identified as the key barriers at play for HPV vaccination (41). These multidimensional barriers are equally relevant to the report’s present investigation into HPV, meningitis, and RSV vaccination, as they may affect the intentions of the vulnerable target groups discussed to get vaccinated for the three infectious diseases.

2. Consent Barriers: HPV, Meningitis, and RSV Vaccination

This report proposes that the various consent barriers to HPV vaccination outlined in the previous section may be expanded and modified to encompass the cases of meningitis and RSV vaccination involving vulnerable groups. In expanding its application to all three vaccination cases, this report proposes recommendations to mitigate the perceived barriers to vaccination among vulnerable individuals.

To ensure culturally relevant vaccine promotion among our target group of children, adolescents, and pregnant women in the context of meningitis and RSV vaccination administration or research, previous research outcomes pertaining to HPV vaccination among vulnerable groups must be expanded. Specifically, physicians and researchers should identify and resolve (or avoid) immunization consent barriers relating to experience, comprehension, advocacy/endorsement, and trust. Additionally, HPV, meningitis, and RSV vaccination administration or research could benefit from a tailored consent process that carefully considers influential behavioural barriers for initiating vaccination among the specific vulnerable target groups. Attitudes and beliefs about vaccine acceptability have been previously investigated, i.e. in the context of young adult women’s perceived barriers to initiating HPV vaccination (41). It is therefore reasonable to expand the scope of the following behavioural barriers to meningitis and RSV vaccination: vaccine cost, pain, safety, side effects, perceived appropriateness to one’s lifestyle (e.g. sexual abstinence), and need for multiple doses.

III. RECOMMENDATIONS

These recommendations highlight the priority needs that should be addressed in the context of informed consent for the administration of vaccines and for the transitional/clinical vaccine research in general (as discussed in Part I) with specific

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13 HPV infection is sexually transmitted and can cause cervical dysplasia (CD) and cervical cancer (CC). Having multiple sexual partners increases exposure to HPV. Intercourse at an early age also exposes the cervix to HPV when it is most vulnerable to infection. (40)

14 See the section on Recommendations for detailed proposals of how physicians and researchers may resolve or avoid these four consent barriers.
emphasize on vaccination cases involving specific vulnerable populations (as discussed in Part II).

By way of improving the readability and design of consent forms for participation in clinical trials of vaccines, along with implementing innovative educational strategies such as “teach-to-goal”\textsuperscript{15}, a complete understanding of consent information has been shown to be achievable with vulnerable, diverse populations especially among those with literacy or language barriers as well as those with a minority status (7, 42).

We now turn to recommendations to address specific immunization consent barriers presented by three categories of vulnerability traits unique among children, adolescents, and pregnant women: cognitive or communicative, social, and legal vulnerabilities.

With regard to accommodating cognitive or communicative needs among our target group, we propose:

1. Drafting consent forms in lay language;
2. Discussing the consent in-person; and
3. Inviting a follow-up with the individual to answer questions at every step of the consent process;
4. Additional recommendations relating to the consent barrier of comprehension (Table 2).

To address the social vulnerability barriers to consent that exist among children, adolescents, and pregnant women, a critical point in addressing discrimination based on age and gender is to first acknowledge that this problem exists. Physicians and researchers must be able to recognize when an individual may be prone to feel discriminated against in the context of vaccine administration or research: cases where a pregnant woman (or young person) may be inadequately informed in the consent process owing to a physician’s or researcher’s prejudicial attitudes against women (or prejudicial presumptions that an individual under their care is not able to fully understand the information due to their young age. In order to successfully address social vulnerability among vulnerable individuals, physicians and researchers must be held accountable in cases of such blatant discrimination.

Legal vulnerability barriers to consent, especially among infants, preadolescents, and adolescents who are unable to legally consent, can be addressed by obtaining consent from a legal representative. For example, a parent can act as proxy for their child. For pregnant women or parents concerned about their consent creating potential legal repercussions for themselves or their children,\textsuperscript{16} researchers should take steps to legally protect the patients and participants under their care. Unlike doctors or lawyers, researchers do not have the legal privilege of confidentiality with their study participants. In light of this, to help protect the privacy of young individuals and pregnant women enrolled in sensitive vaccine-related research, this report recommends that governments enact laws allowing researchers to obtain exceptional privileges akin to policies on the granting of Certificates of Confidentiality (CoCs). CoCs, which are issued by research facilities and agencies of the United States Department of Health and Human Services (HHS), permit researchers to refuse to disclose identifying information about their participants when subpoenaed by a court of law (43).

As for additional recommendations, the report hopes...

\textsuperscript{15} This is a strategy in which participants must first respond correctly to a series of comprehension questions in order to participate in research or clinical interventions.

\textsuperscript{16} For example, genetic discrimination based on “genetic predisposition or carrier status” may lead to increased vulnerability for them and/or their children.
to identify and resolve or avoid immunization consent barriers relating to experience, comprehension, advocacy/endorsement, and trust, as detailed in Table 2 below. This would apply prior to an individual’s decision to consent to the vaccine administration or research. In doing so, physicians and researchers will have respected the individual’s autonomy, dignity, and privacy as it pertains to their body and their personal health information. This will result in the overall strengthening of meningitis, HPV, and RSV vaccination programs to the benefit of the vulnerable populations discussed.

The final portion of this report discusses the influential behavioural barriers in initiating meningitis, HPV, and RSV vaccination programs among young people and pregnant women, specifically concerns relating to vaccine cost, pain, safety, side effects, perceived appropriateness to lifestyle, and need for multiple doses. In terms of recommendations,

### Consent Barrier Recommendations

<table>
<thead>
<tr>
<th>Consent Barrier</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td><strong>1. Experience</strong></td>
<td>Acknowledge a young person’s or pregnant woman’s meningitis, CD/CC, or RSV experience(s) to help establish appropriate rapport with the target group. In so doing, the approach is two-fold:</td>
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<tr>
<td></td>
<td>1. First, under the presumption that the individual may have had minimal prior experience with preventive medical care through vaccination administration or more directly, to the use of vaccination in clinical research, the potential apprehension by the individual towards participation must be addressed;</td>
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<td></td>
<td>2. Second, it is integral that the individual be given adequate information to ensure full understanding of the implications involved</td>
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<tr>
<td><strong>2. Comprehension</strong></td>
<td>Provide a consent procedure that facilitates an understanding of meningitis, HPV, and RSV and the connection between untreated infections, CD/CC, and poor hand hygiene, respectively. This may be accomplished by either:</td>
</tr>
<tr>
<td></td>
<td>1. Writing consent forms in lay language;</td>
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<td></td>
<td>2. Discussing the consent in-person; and</td>
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<tr>
<td></td>
<td>3. Inviting the individual for a follow-up to answer questions at every step of the consent process.</td>
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If working with patients or participants where capacity to consent is an issue (such as a young child, or a pregnant woman limited by a mental defect or disorder), it may be necessary to:

1. Include a procedure to assess the individual’s capacity to consent; and
2. If capacity is deemed not to exist, obtain consent from a surrogate or proxy legally responsible for the individual.

### 3. Advocacy/Endorsement

Support parenting strategies and lifestyle practices that reduce and reverse the risk factors that predispose the target group to infection. Such risk factors include:

1. Untreated infections, for meningitis (44);
2. Sexual activity, for CD/CC; and
3. Failure to wash hands, especially before touching one’s child, for RSV.

### 4. Trust

Ensure trust, and thereby cooperation, with the target group, by:

1. Initiating discussions on meningitis, HPV, or RSV immunization; and
2. Clearly explaining the connection between prevention of the infection and its respective immunization.

The interventions adopting an individualized approach to promoting health protective behaviours may be particularly effective in resolving (or avoiding) multidimensional consent barriers to vaccination (45). For example, if a woman were to express general concerns about the safety or effectiveness of the meningitis, HPV, or RSV vaccine, the consent process could be tailored via integration of intervention materials such as tailored educational resources to focus on reducing her concern. Alternatively, if more practical concerns were raised regarding time constraints or the inability to pay for the vaccine, interventions should be aimed at helping the woman find a time best suited to her needs or directing her to other clinics that offer the vaccine at a reduced cost.

With a particular focus on consent practices applied to vaccination research, where ethical challenges exist in the informed consent process, this report recommends that a dynamic informed consent model is most effective. On the individual level, it is conceivable for researchers to keep the vulnerable target groups informed of how their personal health information is being used in current ongoing research, via platforms such as regular newsletters (in print or digital formats),
and/or interactive websites (46-48). Given appropriate privacy safeguards, pregnant women, adolescents, and parents as proxies for their children could thus be provided individual online accounts which they could access to: update their health information and research preferences, review the details of the research projects in which their tissue samples and data are being used, and opt out if desired. This mechanism can equally be used to seek new tissue samples and data for future research projects.

As for practical applications of dynamic consent mechanisms, there has been a shift in the U.S. toward participants and patients having more control with regards to how their data is used in research. Some groups in the U.S. have developed tools to assist research participants to exert more control over data use. A case in point is Sage Bionetworks, a non-profit organization based in Seattle, which has developed and maintains an open-source software called the “Participant Centric Consent (PCC) toolkit” (49). The PCC toolkit facilitates the implementation of a participant-centred consent process into the design of research projects. Specifically, the PCC toolkit promotes both data sharing and participant/patient engagement in research by providing an interactive “e-consent” approach that engages and informs prospective study participants about potential research projects they may participate in. The toolkit has been implemented by five clinical research studies that are currently ongoing in the U.S (at Sage Bionetworks, Stanford University, Icahn School of Medicine at Mount Sinai, and Massachusetts General Hospital) (50-53).

This approach to consent in vaccine research would honour the spirit of informed consent through its dynamic mechanism, offering some level of control to participants. By ensuring that vulnerable subjects have access to relevant information as it arises regarding their participation in both current and future research, researchers are able to keep the initial consent alive throughout the duration of their research. Likewise, from an informational point of view, potential participants to vaccine research studies are equally informed of who the data custodian is (e.g. the research institution), what technical methods have been adopted by the institution to protect their confidentiality (e.g. anonymization), who will have access to the data, and how to withdraw their consent, if desired. Indeed, by implementing a participant-centred informed consent model to vaccine research involving children, adolescents, and pregnant women, researchers will convey all the necessary information in order to allow the participants involved to decide if they want to assume direct and indirect risks (54). As such, dynamic informed consent with participant control would be most appropriate to promote the right to autonomy of the vulnerable groups discussed in current and prospective vaccine research.
There are informed consent challenges (i.e. ethical gaps, barriers, and priority needs) that are unique to certain vulnerable groups, namely preadolescents, adolescents, and pregnant women in the context of vaccine administration and research.

Two categories of challenges exist in informed consent. The first category is comprised of patient-centered challenges. These challenges prevent a research subject from fully understanding the information that the physician discloses. The second category of challenges is comprised of challenges that are process-centered, which are procedural barriers that prevent a physician from obtaining truly informed consent from prospective patients.

The study of three vaccination cases—the meningitis, Respiratory Syncytial Virus (RSV), and Human Papilloma Virus (HPV) vaccines—reveal that informed consent challenges unique to certain vulnerable groups (i.e. children, adolescents, and pregnant women) stem, in part, from perceived barriers relating to: experience; comprehension; advocacy/endorsement; and trust.

The following interventions may be particularly effective in resolving (or avoiding) consent barriers to vaccination: 1) improving the readability and design of consent forms; 2) incorporating education-specific strategies to improve patients’ or participants’ understanding of consent information; 3) initiating discussion of meningitis, HPV, or RSV immunization and clearly explaining the benefits of infection prevention through immunization.

Implementing a dynamic informed consent model with participant control, accompanied by appropriate privacy safeguards would be the most appropriate consent model to promote the right to autonomy of the vulnerable groups discussed in current and prospective vaccine research.
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APPENDIX

1. RESEARCH METHODOLOGY

Key resources used in conducting legal research and to search for primary and secondary sources include CanLII, LexisNexis/Quicklaw, SOQUIJ/Azimut, La Référence, and WestlawNext Canada.

All other legal and non-legal research was conducted using the University of Ottawa Library’s scholarly article databases.

2. DIVISION OF TASKS

The report was written by three (3) students:

› Yasamin Ahmadi,

› Gill Fruchter, and

› Sarah Quayyum

The first section, INTRODUCTION, was written by Yasamin Ahmadi.

Part I, Informed Consent For Vaccination: Universal Principles, was written by Yasamin Ahmadi and Sarah Quayyum.

Part II, Informed Consent for Vulnerable Groups: Priority Needs and Specific Principles, was written by Yasamin Ahmadi, Sarah Quayyum, and Gill Fruchter.

Part III, Recommendations, was written by Gill Fruchter

The final paper was edited jointly by the three students.