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Dimitri Patrinos, Bartha Maria Knoppers, Erika Kleiderman, Noriyeh Rahbari, David P. Laplante et Ashley Wazana

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Résumé de l'article

Le re-contact des mineurs inscrits dans des recherches lorsqu'ils atteignent l'âge de la majorité ou de la maturité afin d'obtenir leur consentement autonome pour poursuivre leur participation est considéré comme une exigence éthique. Cette question a généralement été étudiée dans le contexte des mineurs qui participent activement à la recherche. Cependant, qu'en est-il lorsque le mineur s'est retiré de la recherche ou a été perdu de vue? Les chercheurs peuvent-ils, dans ces circonstances, recontacter le mineur à l'âge de la majorité ou de la maturité afin d'obtenir son consentement à participer à nouveau à la recherche? Dans cet article, nous explorons la possibilité éthique de recontacter les mineurs dont la participation à la recherche a pris fin, une fois qu'ils ont atteint l'âge de la majorité ou de la maturité. En particulier, nous identifions les scénarios dans lesquels la participation d'un mineur à un projet de recherche peut prendre fin et nous discutons des facteurs qui peuvent aider à déterminer cette licéité éthique. Enfin, nous discutons des défis pratiques et éthiques du re-contact et présentons des modèles de re-consentement qui peuvent être utilisés par les chercheurs.

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Re-contact Following Withdrawal of Minors from Research

Dimitri Patrinos[a], Bartha Maria Knoppers[a], Erika Kleiderman[a], Noriyeh Rahbari[b,c], David P. Laplante[b,c], Ashley Wazana[b,c]

Résumé
Le re-contact des mineurs inscrits dans des recherches lorsqu'ils atteignent l'âge de la majorité ou de la maturité afin d'obtenir leur consentement autonome pour poursuivre leur participation est considéré comme une exigence éthique. Cette question a généralement été étudiée dans le contexte des mineurs qui participent activement à la recherche. Cependant, qu'en est-il lorsque le mineur s'est retiré de la recherche ou a été perdu de vue? Les chercheurs peuvent-ils, dans ces circonstances, recontacter le mineur à l'âge de la majorité ou de la maturité afin d'obtenir son consentement à participer à nouveau à la recherche? Dans cet article, nous explorons la possibilité éthique de recontacter les mineurs dont la participation à la recherche a pris fin, une fois qu'ils ont atteint l'âge de la majorité ou de la maturité. En particulier, nous identifions les scénarios dans lesquels la participation d'un mineur à un projet de recherche peut prendre fin et nous discutons des facteurs qui peuvent aider à déterminer cette licéité éthique. Enfin, nous discutons des défis pratiques et éthiques du re-contact et présentons des modèles de re-consentement qui peuvent être utilisés par les chercheurs.

Mots-clés
re-contact, re-consentement, mineurs, consentement, assentiment, recherche, éthique

Abstract
Re-contacting minors enrolled in research upon their reaching the age of majority or maturity to seek their autonomous consent to continue their participation is considered an ethical requirement. This issue has generally been studied in the context of minors who are actively involved in the research. However, what becomes of this issue when the minor has been withdrawn from the research or has been lost to follow-up? May researchers re-contact the minor at the age of majority or maturity under these circumstances to seek the consent of the minor to re-join the research? In this paper, we explore the ethical permissibility of recontacting minors whose participation in research has ended, once they have reached the age of majority or maturity. In particular, we identify scenarios in which the participation of a minor in a research project may end and discuss factors that can help determine such an ethical permissibility. Finally, we discuss the practical and ethical challenges of re-contact and present re-consent models that may be used by researchers.

Keywords
re-contact, re-consent, minors, consent, assent, research, ethics

Affiliations
[a] Centre of Genomics and Policy, Department of Human Genetics, Faculty of Medicine, McGill University, Montreal, Canada
[b] Centre for Child Development and Mental Health, Jewish General Hospital, Montréal, Canada
[c] Lady Davis Institute for Medical Research, Jewish General Hospital, Montréal, Canada
Correspondance / Correspondence: Dimitri Patrinos, dimitri.patrinos@mcgill.ca

INTRODUCTION

The issue of re-contacting minor research participants to obtain their own consent when they reach the age of majority or maturity has been studied in the context of maturing minors who are actively involved in research (i.e., enrolled participants). However, what becomes of this issue when the participation of the minor in the research ends prior to their attaining the age of majority or maturity (i.e., the minor is no longer an enrolled participant)? May the researcher renew contact with the minor after a period of inactivity and seek their consent to re-join the research project? There have been limited discussions of this issue in the literature. However, as longitudinal and biobanking research projects involving minors become more prevalent, the need to explore this question is timely.

Illustrative of the practical relevance of this issue is the example of the Maternal Adversity, Vulnerability and Neurodevelopment (MAVAN) Study, a prospective community-based, pregnancy and birth cohort of Canadian mother-child dyads. The MAVAN Study follows mothers and their children from birth into adulthood and examines pre- and post-natal influences, and their interaction, in determining individual differences in mental health (1). As the MAVAN Study shifts from assessing children and adolescents to young adults, the researchers are now faced with the question of whether it is possible to re-contact young adults whose participation had ended by withdrawal or because the individual had been lost to follow-up. For a longitudinal developmental study that has been collecting data and biosamples from its participants, there is value in trying to retain as many participants as possible. Larger sample sizes not only have greater statistical power, which is important in answering research questions and detecting meaningful effects (2), but there is also great scientific interest in observing the development of participants over time and obtaining information from them at later life stages. In a longitudinal development study such as MAVAN, there is a strong scientific rationale for wanting to re-contact previous participants. It is therefore useful to explore the ethical permissibility of re-contacting previous participants so that prospective assessments of early life experiences can be compared with post-maturity/majority functioning. Accordingly, this paper explores the question of whether and when it is ethically permissible to re-contact previous minor participants to ask them to re-join a research project.

We begin with an introductory overview of re-contact and the capacity-based approaches that determine when a minor becomes capable of providing their own informed consent to research participation. In particular, we will outline how the

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maturity-based approach to determine capacity for re-contact cannot apply where the participation of a minor has ended by withdrawal or where they have been lost to follow-up. Next, we consider three different scenarios in which a minor's participation in a research project may end: 1) the parent (or guardian) withdraws the minor; 2) the minor asks to be withdrawn; and 3) loss to follow-up (attrition). We consider the ethical permissibility of re-contact in each scenario and identify key factors that may influence such permissibility. Finally, we discuss the practical and ethical challenges of re-contact and present re-consent models that may be used by researchers, where ethically permissible. While this article largely focuses on the Canadian ethical and legal landscape, our findings are not unique to Canada and may be generalizable across jurisdictions.

RE-CONTACT AND THE CAPACITY TO PROVIDE INFORMED CONSENT

As previously mentioned, re-contact involves contacting research participants who were enrolled as minors in the research to seek their informed consent to continue their participation in the research when they reach either the legal age of majority or the age of maturity. Paediatric research may include projects that are carried out over extended periods of time, such as longitudinal studies and studies of large population cohorts that may include biobanks (3-5). These types of studies will often collect data and biological samples from minors over time (6). In contrast, in other research, there is no ongoing interaction with the participants who donated their data and biological samples. In both cases, research participants should be given either the right to consent to continue their participation in the research (or to the continued storage of their data or biological samples) or to withdraw the consent their parent(s) or guardian(s) provided on their behalf. Alternatively, they can also simply be notified that they are enrolled in the research and will remain therein unless they opt out (3).

Re-contact is rooted in the principle that informed consent should be viewed as a continuing process (3). Canada's *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (hereafter "TCPS2"), the joint policy of Canada's federal research agencies, states that consent is an ongoing process to be maintained throughout the duration of the research (7, art. 3.3). Therefore, "if the children mature sufficiently to decide on their own behalf (subject to legal requirements), the researcher must seek the children's autonomous consent in order for their participation to continue" (7, p.33). Re-contact should therefore be seen as an extension of this principle.

Recent literature has begun to question the practicality and obligatory nature of an ethical duty to obtain an expressed, explicit re-consent in the context of paediatric biobank donors (3,4,8). Still, the majority view for paediatric research, in general, remains that minor research participants should be given the chance to provide their own informed consent at the age of majority or maturity (9). Moreover, the need for re-contact may vary depending on the type of research being conducted. For example, in the context of research focused on child development and psychopathology, the need for re-contact may be considered of even greater importance (10).

In this paper, we demonstrate that re-contact where the participation of the minor has ended by withdrawal or because of loss to follow-up differs from re-contact where the minor remains enrolled in the research. For one, we argue that the approach used to determine the capacity of the participant to provide informed consent greatly determines whether a researcher may be able to re-contact a former minor research participant. For instance, while some jurisdictions use the legally fixed age of majority as the age at which consent for research participation can be provided, others adopt a maturity-based approach (3).

Within the Canadian legal and ethical landscape, there is a mixed maturity-based and legislative approach in the context of medical treatment and research. The province of Quebec adopts a statutory approach, whereby minors 14 years of age or over may independently consent to participate in research deemed minimal risk by a competent Research Ethics Board (REB) (11, art. 21). Consent for research that is deemed greater than minimal risk must be provided at the legal age of majority (11). In contrast, Ontario adopts a mature minor rule. Overall, Canadian common law provinces adopt the mature minor rule (3), which considers the capacity of the individual minor to understand the research, rather than relying on their attaining the legally fixed age of majority (3,12,13). In short, minor research participants may acquire the maturity and, hence the capacity to consent to participate in a research project, prior to reaching the legal age of majority in their jurisdiction (14).

Other international jurisdictions have also adopted the mature minor approach. The Netherlands, for example, uses a dual consent system, whereby children 12 years of age and older can consent to participate in research, in addition to their parents' consent (3,14). While there are no precise methods of determining a minor's level of maturity (15), they should generally be able to understand the objectives of the research, the associated risks and benefits, study procedures, long-term implications and the level of commitment required (16). Nevertheless, within the biomedical research context, maturity will depend not only upon the participant, but also on the type of research and the level of risk it involves (13). Hence, in the absence of a legislated age of "medical" majority, maturity should be determined on a case-by-case basis (12).

This discussion of capacity is germane to our analysis of re-contact as the mature minor rule could not apply in cases where the participation of the minor has ended in the research. The researcher, having lost contact with the minor, would be unable to evaluate the capacity to provide an autonomous informed consent. Therefore, in the absence of a legislated age of "medical" majority, the biomedical research determination of "maturity" could not occur for re-contact withdrawn minors or those who had been lost to follow-up. Re-contact would therefore not be permitted in the absence of legislation determining the age of majority, subject to REB approval. Based on this precept, we will analyze the ethical permissibility of re-contact, while recognizing the rights of withdrawal of both parents (or guardians) and minors, as well as the right of minors to make their own choices when they become adults.

POTENTIAL RE-CONTACT SCENARIOS AND ETHICAL PERMISSIBILITY

As mentioned at the outset, the focus of this article is on considerations surrounding the issue of re-contact where the participation of a minor in a research project has ended prior to their attaining the age of majority or maturity. As previously stated, this is a novel issue that has received little attention. We therefore presume that most consent forms for research projects involving minor participants have not addressed what may happen if the research team wishes to re-contact the now mature minor or adult after a period of inactivity. Indeed, the issue of re-contact for enrolled participants has generally not been well addressed in consent forms (3). For instance, a 2013 study of Canadian paediatric research consent forms found that nearly half the consent forms reviewed did not contain any clauses addressing the re-contact of minors (3,8). It is therefore probable that researchers wishing to re-contact former minor participants at the age of majority or maturity have not provided for this possibility in their research projects' consent forms. Accordingly, should they wish to re-contact these former participants, they will need to receive guidance from their institutional REB, which will ultimately decide whether re-contact is ethically permissible in the particular situation. Our present discussion will focus on factors that can help determine this ethical permissibility.

Some have argued in the literature that re-contact of minors whose parents provided proxy consent for their participation in an earlier study is not ethically permissible if the parents did not "contemplate such contact when they initially consented to the child's participation" (17). We contend that there may still be an ethical basis for re-contacting former minor participants, even if this was not contemplated in the initial proxy consent, though this permissibility is subject to several considerations and reasonable limits. Most notably, the ability to re-contact a former research participant needs to be framed within both the fundamental right to participate in or to withdraw from research (7,18) and the right to privacy, which includes the right to be left alone. Within a research project such as MAVAN, which studies mother-child dyads, the rights of both the mothers and the children need to be considered. We therefore identify three potential scenarios in which a minor's participation in research may end and consider whether re-contact would be permissible, taking all relevant factors into consideration. In this paper, we identify key factors that may influence the ethical permissibility of re-contact in such a context.

Scenario 1: Parental (or guardian) withdrawal from the research project

Due to lack of capacity, minors are generally considered incapable of fully appreciating the risks and benefits of research participation (6). Accordingly, consent for minors to participate in research is provided by their parent(s) or legal guardian(s) (10,19). In this sense, parents (or guardians) act as the surrogate decision-makers for their children until they reach the age of majority or maturity and gain the legal capacity to make autonomous decisions (9). Nonetheless, as stated in the United Nations *Convention on the Rights of the Child* (20), any such parental decisions must be made in the best interests of the child (BIC) and consider their well-being (art. 3(1)) and their right to be heard (art.12(2)). Moreover, in the paediatric context, it is important to consider not only the immediate interests of the child, but also their future interests, given that children's interests are fluid and evolve over time with age and maturity levels (20,21). Finally, as a child exists in relation to others, familial interests and values and the parent-child relationship must also be factored into the determination of their best interests (22,23). This is especially pertinent in research projects involving both parents and children.

As an extension of their proxy decision-making role, parents (or guardians) have the authority to withdraw minors from a research project should they so choose (4). In light of this authority, we consider whether and how the decision to withdraw a minor from research influences the ethical permissibility of re-contacting the minor once they have reached the age of majority. In particular, we will consider the increasing capacity and rights of minors as they age and the concomitant decrease in the degree of parental authority (14). While it is recognized that parental decision-making can continue to affect minors well into adulthood (8), the scope of parental authority decreases in conjunction with the minor's cognitive development (14). Therefore, where a minor reaches the legal age of majority, parental authority is no longer applicable and the now-adult, having acquired legal capacity, has the right to make their own choices. We therefore argue that re-contact in this scenario can be permissible, subject to certain considerations and limitations which must be evaluated by a REB.

Firstly, when they reach the age of majority, the former research participant should be able to decide whether they wish to participate in research. The literature has long recognized the individual right to participate in research and to have access to the benefits of participating in research (25). Now fully able to provide autonomous informed consent, without parental authority or influence, the now-adult should be offered the choice to re-join the research project in which they had been enrolled as a minor. We argue that the ethical basis of re-contact in this scenario is rooted in the principle of respect for autonomy, which recognizes the former research participant's right to make their own choices and to make decisions about their actions (26). Though parents (or guardians) exercise legal authority over minors, they cannot always make the decisions that the minor would have made had they been capable of providing their own informed consent at the time the decision was made on their behalf (27). Indeed, research has demonstrated that, over time, minors may wish to make different choices than those made for them by their parents (28). The now-adult may wish to re-join the research project from which they were withdrawn and exercise their autonomy in relation to the research project. Moreover, when minors reach the age of majority, they have a right to access their personal health information (17), including information that may have been collected during a research project. One may therefore argue that the now-adult or mature minor should have the right to know about their previous participation in the research project, if they so choose (17).

Conversely, in a research project containing mother-child dyads, such as the MAVAN Study, it is possible that the minor's health information may also include health information collected from the parent (or guardian) (17). While not absolute, children generally do not have the right to access their parents' (or guardians') personal information and the parent's (or guardian's) decision to withdraw themselves from the research must be respected. Indeed, in a mother-child dyad study, it is highly likely that the parent (or guardian) withdrew themselves from the research project as well. A great deal of information about the mother, the child and their relationship would have been collected during the course of the research, inevitably intertwining the information collected from the two participants. Moreover, the parent (or guardian) may not wish for their child to know about their participation in the research. This is especially true if the research entails a certain degree of personal sensitivity (17). Parental privacy rights and the right of the parent (or guardian) to be left alone after withdrawal must be considered. This is especially relevant if researchers wish to make use of information collected from the minor's initial participation in the research project. It should be noted here that Canadian ethical guidelines do not require the destruction of participants' data or biosamples, but rather leave it to researchers to address how participants' information is handled when they withdraw from the research project (7, art. 5.3).

Scenario 2: Minor (who provided assent) asks to be withdrawn from the research project

While minors are generally incapable of providing informed consent to research participation, their capacity does evolve and develop over time (14). The maturity level of minors involved in research can vary greatly, from infants to those close to the age of majority (24), and should be considered when minors enroll in research. Although they generally lack the capacity to make autonomous decisions, minors may still be able to communicate their opinions in a meaningful way by providing their assent or dissent to participate in research (7). Assent is generally understood to be a minor's affirmative agreement to participate in research (29,30). At a minimum, it involves the ability of the minor to understand the significance of the research (7). Though it does not hold legal standing (31), a child's assent, when it can be given, is complementary to parental consent (32) and acknowledges the child's agency (33).

Minors can provide their assent if they are able to understand the purpose of the research in general (7, art. 3.10), understood as age 7 and up (34). Similarly, where the minor is incapable of providing assent (for example, they are too young to be able to understand the general purpose of the research), their assent to continue their participation should be sought once they are able (7). Assent serves as a record of the child's wishes concerning their participation in a research project (14) and, like consent, is a continuous process that, depending on the nature of the research, may need to be reconfirmed throughout the duration of the project (35).

The importance of obtaining assent from minors capable of understanding the research project is enshrined in normative documents such as the TCSP2 (7) and the *Declaration of Helsinki* (18). Obtaining assent, where applicable, may also be supported by the right of the minor "to be heard" in the United Nations *Declaration on the Rights of the Child* (3,20). Where a minor is capable of providing assent and does not agree to take part in the proposed research project, this disagreement or dissent should usually preclude their participation (7,24,36). Dissent may be overridden by the parent(s) or guardian(s) under exceptional circumstances, such as where participation in research is considered the "best medical option" for the minor (24, p.65) or where the "prospect of direct benefit" is only available through research (37). Nevertheless, the general rule remains that if a minor expresses their desire to no longer participate in the research project, their wishes should be respected and they should accordingly be withdrawn from the research project.

Accordingly, it is possible that a minor who initially provided assent to participate in a research project may, at a later point, change their mind and no longer wish to continue their participation. Under current ethical guidelines, this decision should be respected, subject to the exceptions outlined above, and the minor's parents (or guardians) should withdraw them from the research project. Due to the respect that should be accorded to the minor's decision, we argue that re-contact in this scenario should not be ethically permissible. This determination respects the child's expression of their wishes and acknowledges their developing autonomy (24), as well as supporting their right to be heard (3,20). Indeed, subject to the very specific exceptions, this lack of agreement to continue participation in the research project should be treated as definitive and the minor's wishes must be respected (38). Some authors have even suggested that re-contact where the minor has withdrawn may constitute a privacy breach if there was no permission to be contacted in the future (39). We therefore maintain that a dissenting minor's request to be withdrawn from the research should be respected and that there should be no re-contact unless a REB decides otherwise.

Scenario 3: Attrition

Attrition refers to the loss of study participants over the course of a research project (40). Within the context of longitudinal studies, attrition is a common issue and has an impact on paediatric longitudinal cohorts in particular, as these studies investigate development over time (3). Attrition may create bias in longitudinal studies where the "lost" participants differ from those who remain in the study (41,42). This attrition can be attributed to a number of factors, including withdrawal, loss to follow-up, or death of participants (43). For the purposes of this article, attrition differs from withdrawal of participants, as it focuses on the loss of participants in a research project over time due to lack of ongoing engagement. The distinction between active withdrawal by participants and attrition through non-response from participants has been previously made in the literature (44). In such circumstances, since there was no clear withdrawal of the minor from the research project, through either the minor's or the parent/guardian's initiative, re-contact at the age of majority or maturity could be sought in order to

accurately ascertain the wishes of the individual to continue their participation in the research project. Again, this is subject to REB determination and oversight.

DISCUSSION

Re-contacting a former minor research participant to re-join a research project after their participation ended may be of interest to researchers for a variety of purposes. In most cases, this will be for longitudinal studies, which may include biobanks. More specifically, this form of re-contact could only be of interest where researchers have retained (but are not using) data that was collected from the research participant's initial participation in the project and updates are required. Again, under Canadian ethical guidelines, destruction of data or biological samples is not required when participants withdraw from research.

Capacity to provide informed consent can be attained either at a legally fixed age (a majority-based approach) or at the age at which the minor has matured sufficiently to be able to make their own decisions (a maturity-based approach). Where the participation of a minor in a research project has ended due to withdrawal or where they have been lost to follow-up, evaluation of the maturity level of the minor is not possible. This means that re-contact of a former minor research participant, where ethically permissible and with REB approval, can only occur when the minor has reached the legislated age of "medical" majority in their jurisdiction.

Even where it may be ethically permissible, re-contact may still present certain challenges, which researchers must consider before seeking REB approval to re-contact former minor research participants. Indeed, re-contact may not always be a straightforward process and researchers must be cognisant of the challenges this can raise and how they may affect their research projects. Ancillary to the issue of re-contact is that of re-consent and which model researchers should use to obtain the consent of the previous participants to re-join the research project. All these considerations must be factored into researchers' plans to obtain REB approval for re-contact.

Practical and Ethical Re-contact Challenges

A key challenge in re-contacting participants is that it requires considerable time, effort, and financial expenditure on the part of researchers (27). Tracking down previous research participants can be an especially costly and difficult task, particularly if the last known address of the research participant or their contact information has changed over time (4). Moreover, one must also consider the privacy concerns raised in attempting to track down former research participants if there last known address has changed (7). This is notably a challenge in a research project such as the MAVAN Study that collects not only information from the minor, but their mothers as well, who were also participants in the project. This raises the issue of whether researchers may contact the minor's parent(s) or guardian(s) to obtain their contact information once they have reached the age of majority or maturity, as it may be the case that the minor has changed addresses. Generally, we recommend sending a letter to the minor's last known address, *addressed personally to the now-adult minor*, as the least intrusive method of re-contact. However, we argue against personally contacting the parents (or guardians). Given that they most likely were participants as well and would have also withdrawn from the research, their right to be left-alone after withdrawal *must* be respected.

While re-contact may raise many – often burdensome – challenges for researchers, it should be balanced with a number of factors, including feasibility and cost efficiency (3,9). For one, larger sample sizes have greater statistical power, which is important in answering research questions and detecting meaningful effects (2). For research projects which have "legacy" data and biosamples, that is, data and biosamples that had been collected from participants prior to withdrawal or loss due to attrition, re-consent is required for their use (45). The valuable information the retrospective use of this data can bring can also factor into researchers' decisions in seeking REB approval to re-contact and re-consent participants where there are legacy data and biosample sets. Within the paediatric longitudinal research context especially, data represent specific points in time in the course of the participant's development and are not replicable (46), making this consideration all the more important. Indeed, certain research questions can only be investigated through longitudinal research projects. There is thus scientific interest in observing the development of these participants over time and, hence, obtaining information from them at later life stages.

In short, researchers must consider several practical and ethical factors in assessing whether to submit a re-contact plan to their REB of record. This assessment will be unique to each research project and its specific needs and objectives. However, re-contact should not pose an undue burden to researchers and jeopardize the conduct of their projects. A "middle ground" between the scientific value of re-engaging former participants and resource expenditure should therefore be sought. This balancing act will ultimately decide whether permission to re-contact is worth pursuing for the research team.

Overview of Re-consent Models

Once all relevant factors have been considered and a researcher has obtained REB approval to re-contact former minor research participants, they must decide how to obtain the participant's consent to re-join the research project. The literature presents and describes three primary models of re-consent available to researchers: a) new consent; b) notification with opt-out; and c) waiver of re-consent (3,8,47). These models are generally applied to minors who have reached the age of majority or maturity while actively participating in a longitudinal study. As mentioned above, consent is ongoing throughout the research project and, in Canada, researchers have a duty to seek the minor's autonomous consent for their participation in the research

to continue when they reach the age of majority or maturity (7). Some authors have highlighted the inaccuracy of the term "re-consent" as applied to minors in research, as the minor never provided their consent to participate in the research but rather did so through the consent provided by their parent(s) or guardian(s) (27). Nonetheless, the use of "re-consent" in this context is widely accepted by the literature (48,49,50). We now consider, for the purposes of our present discussion, how these models may be used in the context of re-consenting former minor research participants.

New consent

Upon reaching the age of majority or maturity, the former research participant may be asked to formally consent to continue their participation in the research project. This approach is employed by the Norwegian Mother, Father and Child Cohort Study (MoBa), which requires explicit consent to remain in the study from children enrolled in the project when they reach 18 years old (3,51). Re-consent may be accomplished by presenting a new consent form which reiterates the initial terms of the proxy consent given by their parent(s) or guardian(s) on their behalf. The research participant would then be asked to re-consent to these terms, as well as the terms for the continuation of the research project. In some cases, these terms may differ from those initially consented to by the parent(s) or guardian(s). For instance, some research projects conduct more invasive procedures on adult participants but not minors. The participant would then be asked to consent to these new terms as part of the new consent.

Alternatively, new consent can also be accomplished through an addendum to the initial consent form signed by the parent(s) or guardian(s). This approach is used by the MUHC Centre for Applied Ethics of the McGill University Health Centre in their template consent form for investigator-initiated paediatric clinical research (52). In the addendum, participants are given the opportunity to review the consent form signed by their parent(s) or guardian(s) when they were first enrolled in the research project and are asked to either consent to their continued participation or to withdraw from the research project. The modalities of how their information will be handled if they choose to withdraw must be specified.

Notification with opt-out

A notification with opt-out model is another possible re-contact approach. Under this approach, notification letters explaining the study are sent to minor participants when they acquire the capacity to provide autonomous informed consent, reminding them of their participation in the original research project (through their parent's or guardian's consent), and informing them of their right to withdraw (3). The efficacy of this approach depends, though, upon participants' contact information remaining valid and up-to-date throughout the duration of their participation.

This approach has been adopted, for example, by Statistics Canada, first in the Canadian Health Measures Survey (CHMS) (3) and now in the Canadian COVID-19 Antibody and Health Survey (CCAHS), which collects questionnaire data and blood samples from participants to better understand how COVID-19 has affected the health of Canadians (53). When minor participants reach the age of 14, they receive a letter asking for their approval to keep their blood sample in the COVID-19 biobank (53). If, at this point, the participant wishes to have their sample removed from the biobank, they must notify the CCAHS team by letter or email (53).

Waiver of re-consent

Though not a model of re-consent *per se*, seeking a waiver of re-consent from a REB is a potential method for researchers to continue to use identifiable information from minor research participants without having to re-contact them (9). Within the American context, Institutional Review Board (IRB) practice is variable, with only some IRBs granting such waivers and others requiring that collected information be destroyed if the minor cannot be reached at the age of majority (9). Within the Canadian context, under the TCSP2, a waiver of re-consent is possible for the secondary use of identifiable information, if the applicable REB determines that certain criteria are met (7, art. 5.5A). It is of note that this is an exception to the general rule that requires re-consent of minors who reach the age of majority or maturity within the context of the research project (7, art. 3.3).

Among the criteria that a REB must evaluate for a waiver are the essential nature of the information to the research and the impossibility or impracticability of seeking the consent of individuals to whom the information relates (7). Mere inconvenience does not constitute impracticability (7). Rather, re-consent must pose an undue hardship or onerousness that could jeopardize the conduct of the research project (7). Seemingly, this would not apply to research that involves ongoing interaction with participants, but instead to research that does not entail continuous interaction, such as certain biobanking projects that make data and biosamples available for future research but that have limited contact with participants (9). Examples of impracticability given in the TCPS2 include situations where participants are likely to be deceased, are geographically dispersed, or are difficult to track (7). Impracticability may be further heightened where significant time has lapsed since the participant's initial consent or, in the case of longitudinal studies, their most recent consent. Generally, re-consenting minors upon reaching the age of majority or maturity in a longitudinal study would be considered less onerous by a REB. However, given that in certain circumstances it may be difficult to track down former research participants where their contact information has changed or is not easy to find, re-consent may be considered impracticable and pose an undue burden on researchers, to say nothing of cost. In short, the waiver remains at the discretion of the institutional REB.

Application of Re-consent Models to Re-contact Scenarios

As previously stated, current re-consent models are generally applied to minors who have reached the age of majority or maturity while enrolled in a longitudinal research project. They have yet to be tested in obtaining consent from previous

research participants to re-join a research project. Here, we discuss their applicability in research projects, such as the MAVAN Study, that wish to re-engage previous minor participants. Again, re-contact in this situation can only occur when the minor has reached the legal age of majority in their jurisdiction, as the mature minor rule cannot apply when there is no contact with the minor. Where re-contact is permitted by a REB, researchers may consider that the applicability of the re-consent models depend upon the particular circumstances of their research projects and how the participation of the minor ended.

In the circumstance where the participation of the minor ended due to withdrawal by the parent (or guardian), seeking a new consent would be the most applicable model. After a period of inactivity, a new consent outlining the terms of participation for re-joining the research project would be the most feasible approach in obtaining the informed consent of the former participant. Though beyond the scope of this paper, researchers should be conscious of any potential familial implications where the former participants consent to re-join the research project. In such a case, there may be associated privacy concerns raised for the parent, as exists in research that involves the collection of genetic or genomic information from participants (54).

A notification with opt-out approach would only appear to be applicable where the participant has been lost to follow-up. Under this model, since there was no explicit withdrawal of the participant, they can, upon reaching the age of majority, be notified of their participation via the previous proxy consent given by their parent(s) or guardian(s) (3). Consent to continue participation is implied, unless the participant chooses to explicitly withdraw. This notification approach does not have to wait for loss or withdrawal of a participant, but can also manifest itself in annual updates, birthday cards, etc. that are sent to the minor so as to maintain engagement.

A REB re-consent waiver, which constitutes an exception to the general rule that informed consent is required, could be applicable in either the withdrawal or attrition scenarios. The applicability of this model depends on whether the research project's institutional REB grants a waiver of re-consent. The researchers must be able to demonstrate the impossibility or impracticability of re-contacting the research participants, as well the other required criteria. Additionally, the researchers must still have access to the prior participant's information, which must not have been destroyed or completely anonymized upon withdrawal. Otherwise, a waiver would not be relevant. Where a waiver is sought for data collected from participants who have been lost to follow-up, researchers would not be able to collect prospective information from participants, which may limit scientific value or utility to researchers, depending on their specific projects' objectives.

CONCLUSION

As paediatric longitudinal research projects become more common, researchers may wish to re-contact and re-consent previous minor research participants for numerous reasons of scientific interest to their research project. In this specific situation, we have argued that re-contact could only be possible when the former participant has reached the legal age of majority. The maturity-based approach, applicable to re-contact for enrolled minor participants, is inapplicable where there is no contact with minor, as researchers would not be able to assess the latter's level of maturity.

Working from this premise, we considered different scenarios in which the participation of a minor in a research project may have ended and considered the ethical permissibility of re-contact in each scenario. Where re-contact is deemed ethically permissible by a REB, the former participants can be re-consented either by being asked to provide a new consent or by a notification with opt-out approach. Alternatively, a waiver of re-consent is applicable subject to the fulfillment of certain criteria and REB approval. Nonetheless, there are practical challenges to re-contacting prior research participants that researchers must consider and balance with the scientific value of re-consenting these participants. We hope this discussion serves as a practical guide for researchers when they seek REB approval to re-contact former minor research participants who have reached the age of majority. As a future best practice for research projects for which this could be a relevant issue, we suggest that researchers provide parents (or guardians) the option of consenting to the re-contact of their child at the age of majority or maturity after their participation in the research project has ended, as well as potentially re-contacting the parent(s) or guardian(s) themselves to facilitate re-contacting the minor. This has also been suggested in the literature. In this manner, obtaining consent from the outset minimizes many of the ethical challenges in determining the ethical permissibility of re-contacting the minor at the age of majority or maturity. While this does not eliminate the practical challenges of re-contact, such as change of address of the minor, it serves to streamline and clarify practices for researchers going forward.

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REFERENCES

1. O'Donnell KA, Gaudreau H, Colalillo S, et al. The maternal adversity, vulnerability and neurodevelopment project: theory and methodology. The Canadian Journal of Psychiatry. 2014;59(9):497-508.
2. Guo Y, Logan HL, Glueck DH, Muller KE. Selecting a sample size for studies with repeated measures. BMC Medical Research Methodology. 2013;13(1).
3. Knoppers BM, Sénécal K, Boisjoli J, et al. Recontacting pediatric research participants for consent when they reach the age of majority. IRB. 2016;38(6):1-9.
4. Hartsock JA, Schwartz PH, Waltz AC, Ott MA. Anticipatory waivers of consent for pediatric biobanking. Ethics & Human Research. 2019;41(2):14-21.
5. Poulain T, Baber R, Vogel M, et al. The LIFE Child study: a population-based perinatal and pediatric cohort in Germany. European Journal of Epidemiology. 2017;32(2):145-58.
6. Dove ES, Avard D, Black L, Knoppers BM. Emerging issues in paediatric health research consent forms in Canada: working towards best practices. BMC Medical Ethics. 2013;14(1).
7. Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council. Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. Ottawa, ON: Government of Canada; 2018.
8. Berkman BE, Howard D, Wendler D. Reconsidering the need for reconsent at 18. Pediatrics. 2018;142(2): e20171202.
9. Brothers KB, Wilfond BS. Research consent at the age of majority: preferable but not obligatory. Pediatrics. 2018;142(2): e20173038.
10. Villanueva AG, Majumder MA. Hashtag who's missing? Lessons for genomic databases. Disability and Health Journal. 2021;14(1):100945.
11. *Civil Code of Québec*, CQLR c CCQ-1991.
12. Jeremic V, Sénécal K, Borry P, Chokoshvili D, Vears DF. Participation of children in medical decision-making: challenges and potential solutions. Journal of Bioethical Inquiry. 2016;13(4):525-34.
13. Kleiderman E, Thompson R, Borry P, Boily A, Knoppers BM. Doping controls and the 'Mature Minor' elite athlete: towards clarification?. International Journal of Sport Policy and Politics. 2020;12(1):179-87.
14. Dalpé G, Thorogood A, Knoppers BM. A tale of two capacities: including children and decisionally vulnerable adults in biomedical research. Frontiers in Genetics. 2019;10:289.
15. Cherry MJ. Adolescents lack sufficient maturity to consent to medical research. The Journal of Law, Medicine & Ethics. 2017;45(3):307-17.
16. Cheah PY, Parker M. Are children always vulnerable research participants?. Asian Bioethics Review. 2015;7(2):151-63.
17. Paquette ET, Ross LF. Consent is the cornerstone of ethically valid research: Ethical issues in recontacting subjects who enrolled in research as a minor. The American Journal of Bioethics. 2015;15(10):61-3.
18. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama. 2013;310(20):2191-4.
19. Rahimzadeh V. Sharing outside the sandbox? The child's right to an open data sharing future in genomics and personalized medicine. In: Verma M, Barh D, eds. Progress and Challenges in Precision Medicine. London, UK: Academic Press 2017. p. 171-185.
20. United Nations. Convention on the Rights of the Child. New York: United Nations; 1989.
21. Carbonnier C. Les notions à contenu variable dans le droit français de la famille. In: Perelman C, vander Elst R, eds. Les notions à contenu variable en droit. Brussels: Emile Bruylant; 1984. p. 99-112.
22. Salter EK. Deciding for a child: a comprehensive analysis of the best interest standard. Theoretical Medicine and Bioethics. 2012;33(3):179-98.

23. Brothers KB, Lynch JA, Aufox SA, et al. Practical guidance on informed consent for pediatric participants in a biorepository. Mayo Clinic Proceedings. 2014; 89(11):1471-1480.
24. Council for International Organizations of Medical Sciences. International ethical guidelines for health-related research involving humans, 4th Edition. Geneva: Council for International Organizations of Medical Sciences; 2016.
25. Elks ML. The right to participate in research studies. The Journal of Laboratory and Clinical Medicine. 1993; 122(2):130-6.
26. Beauchamp TL, Childress JF. Principles of Biomedical Ethics. 7th ed. New York: Oxford University Press; 2013.
27. Giesbertz NA, Bredenoord AL, van Delden JJ. When children become adults: should biobanks re-contact?. PLoS Medicine. 2016;13(2):e1001959.
28. Singleton MK, Moon M, Jorgensen EV. Beyond biobanking: future use of specimens and data from pediatric participants. The Journal of Pediatrics. 2020;221:S49-52.
29. Miller VA, Nelson RM. A developmental approach to child assent for nontherapeutic research. The Journal of Pediatrics. 2006;149(1):S25-30.
30. Roth-Cline M, Nelson RM. Parental permission and child assent in research on children. The Yale Journal of Biology and Medicine. 2013;86(3):291-301.
31. Kong CC, Tarling TE, Strahlendorf C, Dittrick M, Vercauteren SM. Opinions of adolescents and parents about pediatric biobanking. Journal of Adolescent Health. 2016;58(4):474-80.
32. Oulton K, Gibson F, Sell D, Williams A, Pratt L, Wray J. Assent for children's participation in research: why it matters and making it meaningful. Child: Care, Health and Development. 2016;42(4):588-97.
33. Rahimzadeh V, Schickhardt C, Knoppers BM, et al. Key implications of data sharing in pediatric genomics. JAMA pediatrics. 2018;172(5):476-81.
34. Hammer MJ. Consent and assent in pediatric research: whose right is it anyway. Oncol Nurs Forum. 2016;43(3):281-3.
35. Rahimzadeh V, Sénécal K, Kleiderman E, Knoppers BM. Minors and incompetent adults: A tale of two populations. In: Illes J, ed. Neuroethics: Anticipating the Future. Oxford: Oxford University Press. 2017. p. 1-27.
36. Bos W, Westra A, de Beaufort I, van de Vathorst S. To stop or not to stop: dissent and undue burden as reasons to stop participation in paediatric research. Journal of Medical Ethics. 2017;43(8):519-23.
37. Ross LF. Informed consent in pediatric research. In: Children in Medical Research: Access versus Protection. New York, NY: Oxford University Press; 2006. p. 87-103.
38. Dockett S, Einarsdottir J, Perry B. Young children's decisions about research participation: Opting out. International Journal of Early Years Education. 2012;20(3):244-56.
39. Ries NM. Growing up as a research subject: ethical and legal issues in birth cohort studies involving genetic research. Health Law Journal. 2007;15:1.
40. Bennetts SK, Love J, Hackworth NJ, et al. Selective attrition in longitudinal studies: effective processes for Facebook tracing. International Journal of Social Research Methodology. 2021;24(2):135-47.
41. Gustavson K, von Soest T, Karevold E, Røysamb E. Attrition and generalizability in longitudinal studies: findings from a 15-year population-based study and a Monte Carlo simulation study. BMC Public Health. 2012;12(1):1-1.
42. Mein G, Johal S, Grant RL, Seale C, Ashcroft R, Tinker A. Predictors of two forms of attrition in a longitudinal health study involving ageing participants: an analysis based on the Whitehall II study. BMC Medical Research Methodology. 2012;12(1):1-7..
43. Young AF, Powers JR, Bell SL. Attrition in longitudinal studies: who do you lose?. Australian and New Zealand Journal of Public Health. 2006;30(4):353-61.
44. Hens K, Van El CE, Borry P, et al. Developing a policy for paediatric biobanks: principles for good practice. European Journal of Human Genetics. 2013;21(1):2-7.
45. Wallace SE, Kirby E, Knoppers BM. How can we not waste legacy genomic research data?. Frontiers in Genetics. 2020;11:446.
46. Beauvais MJ, Knoppers BM. Coming out to play: privacy, data protection, children's health, and COVID-19 research. Frontiers in Genetics. 2021;12:524.
47. Mascalzoni D, Dove ES, Rubinstein Y, et al. International Charter of principles for sharing bio-specimens and data. European Journal of Human Genetics. 2015;23(6):721-8.
48. Hens K, Cassiman JJ, Nys H, Dierickx K. Children, biobanks and the scope of parental consent. European Journal of Human Genetics. 2011;19(7):735-9.
49. Burke W, Diekema DS. Ethical issues arising from the participation of children in genetic research. The Journal of Pediatrics. 2006;149(1):S34-8.
50. Resnik DB. Re-consent upon reaching the age of majority: ethical issues. Journal of Clinical Research Best Practices. 2014;10:2.
51. The Norwegian Mother and Child Cohort Study. Protocol. Oslo: Norwegian Institute of Public Health; 2019.
52. McGill University Health Centre. Templates. Montreal, QC: The MUHC Centre for Applied Ethics; 2020.
53. Statistics Canada. Canadian COVID-19 Antibody and Health Survey (CCAHS). Ottawa, ON: Government of Canada; 2020.
54. Knoppers BM, Kekesi-Lafrance K. The genetic family as patient?. The American Journal of Bioethics. 2020;20(6):77-80.