
Incidental Findings in Pediatric Research

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Incidental research findings, as defined in this symposium's consensus paper, are unexpected findings discovered in the course of research but "beyond the aims of the study."¹ These include findings generated by research methodology, such as imaging or genetic analysis, findings related to clinical screening for inclusion or exclusion, or direct observations of physical abnormalities or behavior. Decisions about managing incidental research findings involve important ethical considerations regarding a researcher's obligations to provide care, minimize harms, and respect research participants' wishes. When the research participant is a child, the triadic relationship between the researcher, child participant, and parent makes these considerations more complicated. (See Figure 1.)

Parents play a critical role in making decisions about their children in all contexts, including research. However, researchers (guided by Institutional Review Boards [IRBs]) play a larger role in deciding what benefits and risks children should be exposed to in the research setting than the role they play in research with adults.² This larger role is based on the ethical concern that parents, acting as surrogate decision makers, have the potential to make decisions that may be counter to the interests of the child, who cannot speak on her own behalf. A researcher's role can become even more complicated when an older child speaks up and expresses a view that is contrary to her parent's view.

The distinction between incidental findings that have clear and proximate clinical importance (clinical utility)³ and those whose clinical importance is unclear, unlikely, or distant is particularly relevant. For incidental findings *without* clear and proximate clinical importance, a significant question is whether there should be disclosure to either parent or child. For incidental findings *with* clear and proximate clinical importance, when there is agreement within the research team that the information should be disclosed, the question in the pediatric context is to choose between disclosure to the parent or to the child. It is possible that a parent or child may not want to know information related to an incidental finding. More importantly though, when either parent or child *does* want information about incidental findings, one of them may want to limit how that information is shared.

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(Parents may not want to share with children and vice versa.) For example, with an adult-onset genetic disease, a parent might want to know that a child carries the gene but may not want to disclose this information to the child because the parent may be concerned that the information will be upsetting to her. Conversely, for a recessive condition, an adolescent might want to know that she carries a gene, but may not want her parent to know because the information will have implications about reproductive decision making that the adolescent might want to keep private. The central question becomes whose wishes should prevail when parent and child have different views about disclosure or sharing the information with each other.

This paper discusses whether incidental findings about children should be disclosed at all, under what conditions, and to whom. These questions should be considered within the general frameworks for pediatric health care decision making and pediatric research participation. The answers to these questions will depend on the clinical significance of the information, the family context, and pragmatic feasibility.

Parental Decision Making for Clinical Care and Research

Parental authority for clinical decision making generally rests on two pillars. First is the parental interest in “self-determination” that generally extends to decisions about their children. Parents express this self-determination in where they choose to live, what they eat, how and whether they practice a religion, how they school their children, and in which extracurricular activities their children participate (e.g., sports and music).

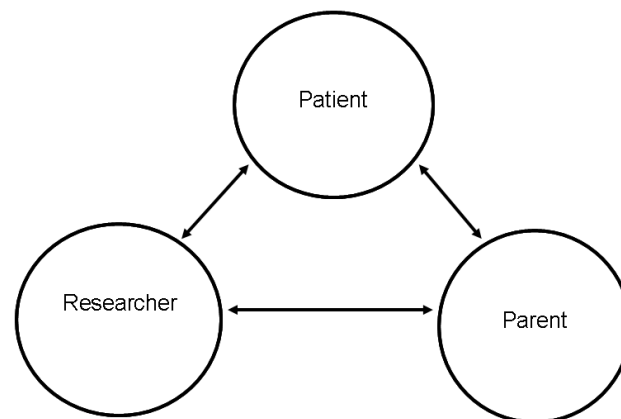
The second pillar is that parents are presumed to be in the best position to determine what is in the child’s interests. Parents may also consider their own interests, their families’ interests, or the community’s interests while making decisions. It is only when parental decision making harms children that state interference is typically justified.⁴

Though parents have considerable latitude in making decisions for their children, third parties may refuse to cooperate. When parents request certain actions from a physician or researcher, the physician or researcher may justifiably refuse the request if the

professional decides that the request is not in the child’s interest. For example, in the clinical context, treatment of children is given over parental objection when there is a high risk of irreversible harm if no treatment is given. Similarly, providers typically will not prescribe antibiotics, order magnetic resonance imaging (MRI) scans, or obtain certain genetic tests unless there are clear clinical benefits, even if a parent requests those interventions. Of course, there are many clinically ambiguous circumstances in which clinicians will defer to parental requests precisely because of the parents’ otherwise central role in making decisions for their children.

Figure 1

Triad of Communication in Pediatrics



Parental decision making in health care is challenged most effectively by the children themselves, as they become cognitively and affectively more mature. Disagreements between parents and adolescents about health care may occur in a wide range of contexts including decisions about end-of-life care, psychiatric treatment, and use of contraception. There is a growing appreciation of the importance of involving adolescents in health care decision making and a willingness to support adolescents’ views that may differ from those of their parents. Further, in many states, case law may permit adolescents to make sensitive health care decisions without the involvement of the parents, such as about treatment of sexually transmitted diseases, care during pregnancy, and treatment for addiction.⁵ However, only a handful of states have

specific laws limiting health information disclosure to parents.⁶

In the research setting, parental decisions to enroll their children in research are limited by which research studies are approved by an IRB to include children. The IRB bases such decisions on the federal research regulations that limit the scope of allowable research, related to an assessment of the benefits and risks of the research.⁷ The federal regulations require that

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pediatric research without a prospect of direct benefit must fall into categories of “minimal risk” (section 404) or “minor increase over minimal risk” (section 406) to be approvable by the IRB. If there is a prospect of direct benefit, then the risks must be reasonable in relationship to the anticipated benefits (section 405).⁸ This determination of risk and potential benefit relates to each particular intervention that may pose risk, rather than being a global determination for the whole study.⁹

How an IRB should respond to a plan about disclosure of incidental findings will depend on its assessment of the risks and potential benefits of disclosing or not disclosing the incidental findings. Those incidental findings with clear and proximate benefit to the child could be considered under section 405 because of the prospect of direct benefit *to the child*. To be approved under section 405, the potential benefit-risk ratio must be “favorable” compared to the alternatives. In considering incidental findings, investigators and IRBs will need to assess what information is important to disclose because of a favorable potential benefit-risk ratio and what information is best left undisclosed to avoid risks of psychological or physical harms for the child. For those incidental findings without clear and proximate clinical importance, the IRB might still use the section 405 framework, particularly if the argument for disclosure was based on the value of the information, even if a benefit was not clear or proximate.

Incidental Findings with Clear and Proximate Clinical Importance

For research involving adult participants, the disclosure of an incidental finding with clear and proximate clinical importance, for example a brain MRI finding suggestive of a significant mass, is not controversial.¹⁰ There may be different views about whether a particular finding has clear and proximate clinical importance, such as being a BRCA1 carrier. But once

clear and proximate clinical importance is established, the consensus paper published in this symposium states general agreement that a plan should be developed by the researchers to provide such research-related findings to participants, and this plan should be communicated to the participants as part of the informed consent process prior to the initiation of the research.¹¹ The primary

purpose of disclosing incidental findings is to convey enough information so that their clinical importance is understood and appropriate referrals for follow-up care can be made.

The approach to disclosure of incidental findings in pediatric research with clear and proximate clinical importance will vary depending on the age of the child. In research involving infants and very young children, information with clear and proximate clinical importance should be treated much as it would in a research situation with an adult participant, except that a parent will be receiving the information rather than the infant or young child. This approach is reasonable because parents are the primary decision makers for very young children in most settings including decisions about medical care and research. As children grow older and their understanding about their health and medical condition improves and their ability to express themselves becomes more proficient, it is important to consider their preferences even though a parent may ultimately have decision-making authority. For this reason, studies involving school-age children and adolescents are more complicated because of the question of whether to provide these findings to the parents, or the child/adolescent, or both.

In general, incidental findings discovered during research that have clear, proximate, clinical importance should be handled similarly to other clear, proximate, and important clinical information discovered during routine health care. Although typically such clinical information is disclosed to both the child/adolescent and the parent, some instances in which one party prefers not to disclose to the other should be respected. For example, there is a legal and ethical

consensus that adolescents can make decisions about treatment for particular conditions (such as sexually transmitted diseases, as discussed above), and it follows that they are also entitled to decide whether to disclose this information to their parents.¹² However, there has also been some discussion in the literature about parental decisions not to disclose a diagnosis to a child because of concern that the information would be upsetting (such as a diagnosis of HIV, cancer, or cystic fibrosis).¹³ Typically such requests are honored as much as the situation allows, even though it may ultimately be better for the child to have an appropriate understanding of her condition.

These two contradictory examples point out that the decision about approaching incidental findings with clear and proximate clinical importance may also depend on both the nature of the information and the family context. Nevertheless, we would support a general “rule of thumb” to present such medical information to both the parent and the school-age child or adolescent. The intention to do this should be relayed to the parent and child/adolescent during the informed consent process in order to communicate the mechanism and scope of disclosure should an incidental finding arise. This way, they will have the opportunity to refuse to participate in the research, if they wish.

Disclosing important clinical information about children to both the parent and the child/adolescent together treats the child/adolescent and the parent with equal respect. This approach also has the pragmatic value of avoiding the opportunity for either the parent or child to request non-disclosure to the other, a request that may add to the complexity of the situation. However, disclosure to both does not facilitate further discussion with one of the parties, in private, at the time of the disclosure. Secondly, it limits the opportunity for one party to prepare the other emotionally for the disclosure. Finally, it prevents one person from being in a position to decide whether or not to inform the other party. At times it may be difficult to appreciate which situations will be considered problematic by the parent or the child/adolescent because of personal views, since not all such situations involve emotionally charged or life-threatening information. However, when the considerations above appear to be relevant and important, an *initial* disclosure to only one party may be most appropriate, even if the agreed upon plan was for disclosure to both.

Deciding who should get relevant information first may not be as important an issue as the decision about when the researcher intends to eventually disclose the information to both the parent and child. Of course, both might prefer to hear the information first, which

may create ambiguity about whom to disclose information to initially. Disclosure to each then becomes an issue of timing. The researcher must assess the situation and ultimately choose one party to receive clear, proximate, and clinically important information first.

The decision about the order of disclosure is more important when the researcher would be willing to honor a request to withhold information from the other party. In such cases, it is important for the researcher to discuss the pragmatic limitations of non-disclosure with the person requesting that the information be withheld. For example, if the researcher is asked about a particular finding, such as a positive drug test, even the response that this information cannot be disclosed may itself imply that there was a (positive) finding. A second concern is that staff and technicians may inadvertently disclose the finding, not realizing that the child or parent is not aware. For example, if a 10-year-old child is in a study for HIV patients and has not yet been informed that she is HIV-positive, then a phlebotomist could make references to AIDS without knowing that the child is unaware of her diagnosis. Finally, in some circumstances, non-disclosure is simply not feasible because the finding may be physically apparent (e.g., near-term pregnancy) or its presence deducible (e.g., diseases requiring intensive treatment).

Initial Disclosure to Adolescents: Relaying Sensitive Information

There are a number of clinical circumstances (such as pregnancy, sexually transmitted disease, drug use, and psychiatric issues) in which clinicians routinely offer adolescents promises of confidentiality. However, these conditions may be discovered in research as incidental findings. Many research studies use clinical testing instruments including pregnancy tests, toxicology screens, and psychiatric inventories as part of the screening for the study. Incidental findings resulting from these testing instruments in pediatric research are likely to be the most frequent and challenging.

In the clinical context, adolescents are offered confidentiality of results with no disclosure to their parents,¹⁴ based on respect for the adolescent and to encourage adolescents to seek health care, as supported by case law and statutes.¹⁵ In the research context, the federal regulations on human subjects research permit adolescents to participate in research without parental permission when the study concerns a “condition or population for which parental permission is not reasonable to protect the child.”¹⁶ These criteria are commonly understood to permit research about contraception or drug use without parental per-

mission.¹⁷ However the regulations focus on parental permission for enrollment in a particular study, not specifically for certain aspects of a study. For example, the regulations would permit the waiver of parental permission for a study of contraception practices among adolescents but not a pharmaceutical study for asthma, even if the study also included a pregnancy test as a screening tool prior to study enrollment. The health risks of an asthma trial would justify parental permission for the study, including permission for the pregnancy test.

Handling sensitive clinical information in adolescents in the research setting is more complicated than it is in a clinical setting. It is always advisable to disclose any sensitive information, including incidental findings, to the adolescent first, particularly if there is concern that disclosure to the parent could trigger abuse or other harm to the adolescent. When a promise of confidentiality has been made to the adolescent, it is still appropriate to encourage her to disclose sensitive information to at least one parent, particularly when the parents are her best resource for support. On the other hand, such promises of confidentiality should not necessarily be extended to sensitive *inci-*

consent form that such information might not be kept confidential may not sufficiently warn an adolescent to avoid placing herself in a situation that may reveal an undesirable finding. It is advisable to have a direct conversation with the adolescent about limits of confidentiality prior to initiation of the research study.

Second, although the approach to adolescent confidentiality in clinical care is generally designed to encourage adolescents to seek care, sometimes the approach in research may be intended to discourage participation. In some research studies, for example, where the primary concern is enrolling adolescents who will complete the study, planning to share incidental findings with parents may be an important approach to discourage adolescents with risky behavior from enrolling. Advising an adolescent that this type of information would be disclosed to parents may be the most direct way to get adolescents to understand the risks of disclosing such incidental findings to their parents. In other research studies that may provide the best clinical option for a rare disease, protecting the confidentiality of incidental findings may be important to encourage adolescents to enroll in research.

At times it may be difficult to appreciate which situations will be considered problematic by the parent or the child/adolescent because of personal views, since not all such situations involve emotionally charged or life-threatening information. However, when the considerations above appear to be relevant and important, an *initial* disclosure to only one party may be most appropriate, even if the agreed upon plan was for disclosure to both.

dental research findings. Of course, in a research study for which the parent *did not* give permission, this information should remain confidential. However, a number of differences between the research and clinical contexts justify not promising confidentiality for certain incidental findings.

First, it may be pragmatically difficult to keep some information confidential from the parent. For example, if an incidental finding of drug use or pregnancy would require that an adolescent be terminated from the study, a parent may confront the researcher or her adolescent to understand the reason behind the termination. In a research setting that requires parental permission, confidentiality may be impossible to maintain when parents have access to medical records. Thus, a promise to keep such information confidential would be misleading. Even a written disclosure on a

Adolescents and parents need to agree to the conditions of the study (if parental permission is required). Some parents could agree to enroll their child in a study with an understanding that certain information would be withheld from them, but other parents might not give permission to enroll their adolescent in research without an agreement that clinically important information about pregnancy or drug use would be disclosed to them. Similarly, an adolescent's decision to enroll might depend on the approach taken to protect her information in the study.

We believe that it is appropriate to obtain permission from parents for tests and procedures that might produce sensitive information, and to plan to disclose any incidental findings to both the parent and the adolescent. We offer the following suggestions directed toward achieving the primary objective of promoting

the well-being and respect of the adolescent. First, a researcher should clearly and explicitly inform both the adolescent and the parent in the consent process that sensitive, clear, proximate, clinically important information will be disclosed to both of them. Second, as part of the parental permission and adolescent assent process, the researcher should speak with the adolescent alone and explain that one component of the assent process is to give the adolescent a chance to decline participation without her parent present. When the adolescent is alone with the researcher, it can be reiterated that the study will include pregnancy or drug testing and that the result will be disclosed to the parent. The researcher should remind the adolescent that she is entitled to decline participation in the study for any reason, and should ask again if she really wants to be in the study.

Undoubtedly, there will still be positive pregnancy and drug tests in adolescent research subjects. By opting to disclose such findings first to the adolescent, it may be possible to create an alliance with the adolescent to involve the parent in these clinically important issues. This approach also permits the adolescent to identify extenuating circumstances to the researcher, such as abuse or fear of abuse, which would preclude disclosure to the parent.

Initial Disclosure to Parents: Relaying Serious Information

Some incidental findings will suggest serious illnesses such as a complete blood count (CBC) indicating leukemia or an MRI scan showing a brain tumor. It is reasonable to first discuss such serious incidental findings with the parent. It may be necessary to disclose such findings to the child in an age-appropriate manner to proceed with treatment. Revealing the finding to a parent first, however, allows the parent to ask questions and collaborate with the researcher on the best way to discuss the information with the child. It may also give the parent time to process the information emotionally, so that she can then focus on helping the child/adolescent understand the information, rather than both having to process the information themselves at the same time.

This approach is probably most important in the context of disclosures about serious conditions. Parents may have different thresholds regarding what sort of information would warrant this approach, rather than the standard joint disclosure that typifies pediatric interactions. During the consent process, when the issue of incidental findings is discussed, the researcher may ask the parent if she has any preferences for initial disclosure of serious incidental findings that are uncovered.

When a researcher discloses to a parent an incidental finding with clear and proximate clinical importance, the main emphasis will be on providing referrals for appropriate clinical follow-up. It will also be important to talk to the parent about how to best disclose the information to the child. Because most parents will have limited experience discussing such information, the researcher can offer to coach the parent, directly disclose the information to the child, or involve a clinician with experience disclosing this type of clinical information to talk with the parent or child. In some cases, the disclosure to the child can be deferred until the family meets with a clinician for clinical evaluation.

Although the focus here is on serious incidental findings, such as cancer or HIV, some incidental findings will raise grave concern before reaching a clear diagnosis. Communication about such findings has added complexity due to the uncertainty of the meaning of the findings. However, because the child will be directly involved in the further clinical evaluations, it is generally reasonable to explain to both the parent and the child the source of the concern and what the next steps should be.

Incidental Findings without Clear and Proximate Clinical Importance

When incidental findings do not have clear and proximate clinical importance that requires further clinical evaluation, follow-up, or treatment, there may still be obligations to offer the findings. The argument for offering this information rests on the principles of respect and reciprocity.¹⁸ The central claim is that research participants should be provided with research findings (incidental or otherwise) if the results are meaningful to them. One justification for this claim is an obligation of “reciprocity,” which is related to research participants contributing their time and their bodies to the research in exchange for information about themselves. Further, the value of the information is not objectively defined but rather has “subjective value” defined by each participant. Since all research participants will not have the same preferences, unlike information with clear and proximate clinical importance, information with potential value to the participant should be *offered* to allow participants to express their preferences on whether to receive it.

While concepts of “reciprocity” and “subjective value” provide the basis of *prima facie* obligations, countervailing concerns may attenuate the obligation to offer this information,¹⁹ including concerns about psychosocial risks to the participants and their families and physical risks (if the information were to

result in erroneous clinical decisions), and concerns regarding the researcher's capacity and resources to communicate such information. We will not provide a definitive account of the balance between these competing views with regard to such incidental findings in adults. However, we argue below that in the pediatric context, the balance between these views will generally tilt toward less disclosure because the arguments in favor of disclosure are not as compelling.

First, the reciprocity argument used to justify disclosure in adults takes on the characteristics of an exchange when applied to children in research studies. That is to say, the parent may expect to learn information about her child discovered during the research in return for allowing her child's participation in the study. We are not arguing that such exchanges are inherently problematic, just that these exchanges require careful scrutiny. For example, payment to parents for the participation of their children in research also represents such an exchange.²⁰ Paying parents is considered ethically acceptable, provided that the risks of the child's participation and the payment plan have been reviewed by the IRB and found "reasonable" and the plan is communicated to the parents. However, the arguments to justify some parental payment would not justify any parental payment. There are a range of reasons for limiting the size of payments, including concerns about undue influence on parents and parental pressure on children. Similarly, the reciprocity argument may justify disclosure of some information but not necessarily all information. Because of concerns about harms to children and their privacy, greater limits exist on reciprocal obligations for disclosing incidental findings to parents than to adults about themselves.

Second, the subjective value argument for disclosure is based on the premise that the information may have value to an individual, even if it is not clinically important. Therefore, parents should be able to decide what information is meaningful to them rather than have the decision made by researchers or IRBs. However, parents may have different views about what information is important, compared with the information their children value. A paradigmatic example is research findings of the Apolipoprotein allele 4 (Apo E 4) that might suggest an increased risk for Alzheimer disease much later in life, for which there is no established intervention in children. Although a parent may want such information about her child, this desire does not

sufficiently justify the researcher providing the information to the parent.

One basis for justifying nondisclosure of this information is found in the "open-futures" argument.²¹ This argument considers the fact that many adults would not want to know certain information that could affect them later in life. Disclosing this information to the child deprives her of the later decision as to whether to receive this information as an adult. Of course, a parent could avoid this problem by not sharing the finding with the child. However, a related concern is that some adult children would also want to keep such information private, even from their parents. Thus, disclosure to a parent prevents the child from being able to keep that information from her parents.

Perhaps the most compelling reason to not disclose incidental findings that do not offer clear and proximate clinical benefit is that the risks associated with disclosing such findings may not be balanced by sufficient benefits to justify the disclosure. These risks may include physical risks related to unnecessary

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clinical interventions or psychosocial risks of distress and anxiety related to the information.²² Ambiguous information can encourage misunderstanding about the presence of a disease or misperceptions about the seriousness of a condition.

These arguments have been well rehearsed in the literature on the disclosure of information gleaned from genetic testing in children,²³ and the general argument for non-disclosure of genetic testing results also applies to incidental findings without clear clinical importance, whether they are genetic or not. At the very least, it suggests that parents are not entitled to any incidental finding simply because it is important to them.

Although incidental findings invoke images of unidentified bright objects on a MRI scan or large sequences of DNA of unknown meaning, the pediatric incidental finding that has been discussed most in the literature is the identification of misattributed parentage.²⁴ This finding can result from studies that include

parents and children and may occur in preparation for a transplant, or in some genetic studies. Family members may have varying levels of knowledge about this information and diverging views about whether this information should be disclosed to other family members who are unaware of it.

In some cases, this information will have clear and proximate clinical importance for an individual, particularly if it reveals that a person is not at risk for developing a medical condition or not at risk for having children with a feared condition. However, in most cases, this information will have no clinical significance. The benefits and risks of revealing information about misattributed parentage are psychosocial, difficult to predict, and are unevenly distributed in the family. Thus, many competing interests of the child and the parents need to be considered.

Families should be able to clarify parentage if that is important to them, but we suggest that in the context of a research study, it is not necessary to offer this information merely because it is possible to do so. Families can decide about such testing with the involvement of clinical professionals, or can also obtain such testing using a cheek swab analyzed via private mail-in services.²⁵ Researchers may not be equipped to address the psychosocial complexity surrounding parentage issues. It is reasonable for researchers to plan not to disclose information about misattributed parentage (unless it is clinically important) and to communicate this plan to individuals and families involved in research.

Conclusion

When designing a study, investigators must develop a plan that adequately addresses handling incidental findings while considering the rights and welfare of participants. This plan should begin with identifying incidental findings that may result from screening processes or the research process itself, such as analysis of radiology images or genetic material. The identified findings should then be categorized into those of clear and proximate clinical importance and other findings. Following categorization, a plan should be developed to disclose clear, proximate, clinically important information to the child/adolescent and/or her parent.

Our recommended default approach for handling incidental findings of clear and proximate clinical importance is to disclose to both the child/adolescent participant and her parent. In most cases, it may be best to disclose such information to both at the same time but, in some cases, it may be appropriate to disclose sensitive information such as pregnancy to adolescents first and serious information such as a cancer diagnosis to parents first.

For incidental findings without clear and proximate clinical importance, it is best to plan for no disclosure until there is further discussion between the researcher and the IRB. This discussion should focus on the potential clinical value of the information, any risks of disclosure or nondisclosure, and how to maximize benefits and minimize risks. In some cases, ambiguous information, whose informative value may increase as data emerge, may be sufficiently meaningful that some families would want this information, while others might not. Unlike information with clear and proximate clinical importance, this type of information should be “offered” rather than simply disclosed to allow families to express their preferences.

Once a plan for handling incidental findings is developed, it is important to communicate this plan to participants and their families. Such a plan should favor the needs of the child/adolescent participants while respecting the needs and requests of their parents as much as possible. It may not be sufficient to disclose the plan in the consent form because the participants may not be familiar with this topic and the concerns surrounding it. Particularly when dealing with adolescents who may have different views about disclosure of incidental findings than their parents, it is important to have a private conversation with them to ensure they understand and agree with the plan about how such information will be handled if they enroll in a study that anticipates such findings.

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