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# How do parents decide on genetic testing in pediatrics? A systematic review

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**ABSTRACT**

**Purpose:** This systematic review aims to identify factors that influence parents' decisions regarding pediatric diagnostic and predictive genetic testing (DT/PT). Factors are integrated into a conceptual model of decision-making. Implications for genetic counseling, research, and ethics are derived.

**Methods:** PubMed, PsychInfo, WebofScience and references of related reviews were searched for original publications between 2000 and 2023. Extracted factors were categorized into an existing model.

**Results:** Of 5843 publications, 56 met inclusion criteria. The included studies differentiate between DT, traditional, and expanded PT and describe factors impacting parental decisions on both to have the child genetically tested and to be informed about additional findings. Factors included: 1. benefits/hopes, 2. worries/concerns, 3. values and beliefs, 4. individual circumstances, and 5. emotional states.

**Conclusion**: Our work extends an existing empirical decision model of family decisions about genome sequencing to genetic testing in pediatrics in general, adding the categories "individual circumstances" and "emotional states". The factors can be further integrated into the Health Belief Model; the importance of emotional states is reflected in dual-process theories, such as Fuzzy Trace Theory. Research is required on emotional states, differences between DT and PT, parents' decisions about result disclosure, and dyadic variables as decision-making predictors.

**Keywords**: genetic testing, predictive, diagnostic, parents, decision-making

## INTRODUCTION

Genetic testing in pediatrics is becoming more common both for diagnostic purposes (diagnostic genetic testing, DT) and for predictive purposes (predictive genetic testing, PT).[1] PT traditionally refers to genetic testing of asymptomatic children at risk for a genetic disease due to family history (traditional PT). PT is also being used for healthy children with no family history in research studies, including those of genomic newborn screening (gNBS) (expanded PT). In this article, the term "genetic testing" refers to single gene/gene panel testing and exome and genome sequencing.

Parental decision-making on genetic testing for their child can be a sensitive process, involving choices made in the child's best interest with potential impacts on their life and on other relatives.[2] Emotional challenges, such as guilt, anxiety, and decisional conflict, as well as emotional reactions during the testing procedure can place additional burden on parents.[3] Testing a non-symptomatic child can increase this complexity.[4,5] PT involves complex estimates of disease probability, and low to moderate penetrance may increases the uncertainty concerning the clinical impact of a certain genotype.[6] Furthermore, emerging capabilities for testing entire exomes or genomes produce even larger amounts of information and involve additional decisions regarding which results should be reported and whether parents should be able to choose which types of their child's results to receive, such as adult-onset conditions or (non) actionable secondary findings.[7] This complexity of parental decisions about pediatric genetic testing requires the consideration of a psychological perspective on factors that impact parents' decision-making.

Recently, Smith et al[8] presented a comprehensive model that describes the key drivers of caregiver decision-making regarding pediatric genome sequencing. The model posits that values influence the perceived benefits, risks, and pragmatic considerations of pediatric genome sequencing and includes both child- and family-related factors. The model was

developed based on a qualitative analysis of semi-structured interviews with 41 caregivers of children with suspected genetic conditions. The model's advantages include the consideration of a wide range of influencing factors and complexity through different levels, as well as the emphasis on individual values in decision-making. The authors utilize it as a foundation for the development of a discrete choice experiment. Given its holistic nature, we assume that the model can also be transferred to other contexts of family decisions and can enhance our comprehension of family decision-making processes.

Our aim is twofold: firstly, to identify pertinent emotional, relational, and contextual factors that influence parental decisions regarding genetic testing in both the DT and PT contexts. This encompasses both decisions to undergo testing and decisions regarding the receipt of results that come along with genome testing options. We selected this broad field of contexts and decision types to enable a holistic understanding of the factors at play. The investigation of the factors influencing decision-making in both DT and PT settings, as well as the analysis of different types of decisions, can inform the development of educational materials, supportive interventions, and genetic counseling. Secondly, we seek to determine whether these factors can be integrated into the model proposed by Smith et al,[8] and, if necessary, to augment the model to accommodate the expanded scope of applications. In order to achieve these objectives, a systematic review was conducted.

Previous reviews have addressed similar themes, such as parents' attitudes toward genetic testing excluding exome or genome sequencing, differentiating between tests with clinical benefit, no apparent benefit and hypothetical testing scenarios.[9] Reviews also explored interest and decision-making in specific genetic contexts, such as prenatal testing,[10] gNBS,[11] dyadic decision-making on genetic testing,[12] and adult genetic testing.[13,14] This review constitutes a significant contribution to prior literature, owing to its comprehensive exploration of the diverse field of application and its incorporation into the empirical framework proposed by

Smith et al.[8] Additionally, our exclusive emphasis on actual rather than hypothetical factors enhances the practical significance of findings.

## MATERIALS AND METHODS

### Search Strategy

We conducted a systematic search for publications addressing our objective following the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) 2020 statement[15]. Reporting adheres to PRISMA guidelines (checklist provided in Supplemental Table 1) and SWiM[16] (Synthesis Without Meta-analysis) guidelines (checklist provided in Supplemental Table 2). The initial search took place in January 2023 within the databases PubMed, PsychInfo, and WebofScience. Additionally, we searched the reference lists of 11 eligible reviews. We updated the search in December 2023. Search terms to describe parents were combined with terms related to genetic testing and decision-making. We provide our detailed search terms in the Supplementary Search Strategy. The search was limited to publications since 2000, because sequencing the human genome was mostly complete by early 2000.[4]

### Article Selection

Inclusion criteria were 1) primary research articles reporting qualitative, quantitative and mixed-method studies on 2) actual decisions made by parents on genetic testing of their child, providing 3) factors contributing to parents' decisions in the context of 4) pediatric genetic testing (DT or PT). We excluded studies 1) on hypothetical decisions and more distant variables such as general intentions or attitudes, 2) on settings outside pediatrics, such as prenatal genetic testing, direct-to-consumer testing, testing for medical research purposes only, decisions about adult/parent testing, 3) that were not published in English, 4) published before 2000, and 5) exclusively resulting in publication types such as grey literature, reviews,

short reports, comments, (conference) abstracts, and dissertations. Articles were screened independently by two researchers (ESD and student interns) during title/abstract and fulltext screening. Disagreements were resolved through discussion and consulting a third researcher (SPL). We assigned excluded articles to 5 exclusion categories (see Figure 1).

*[Figure 1 here]*

**Deviations from the pre-registration**

The review was pre-registered at Prospero (ID: 383827). To manage the large number of studies, eligibility criteria were tightened and then deviated from the protocol: 1) merely include actual decisions and exclude hypothetical decisions and more distant variables such as attitudes and opinions, 2) exclude post-testing decisions, to keep decision processes comparable among studies, 3) combine genomic and genetic testing. The consideration of expanded information from genome/exome sequencing is instead represented through the decision to receive additional findings.

**Data extraction and analyses**

E.S.D and student interns (C.K., J.P., M.Z.) independently extracted bibliographic information, study methodology, characteristics of parents and children, parents' decisions and relevant factors for their decisions for both qualitative and quantitative data into a data extraction form in MS Excel.

After extracting factors from the original studies, E.S.D. assigned them to the categories suggested by Smith et al.[8] Characteristics of each study and assigned categories were summarized in tabular form. The assignments were reviewed by E.S.D., J.M., and K.M.S. Factors that did not align with Smith's model were discussed by E.S.D., J.M., and K.M.S. and additional categories were introduced to capture the broader context of DT, PT, as well as diverse decision outcomes (testing and receiving additional findings).

In the synthesis, studies were grouped by decision type and categories proposed by Smith et al[8] and our extension. For the decision to test, factors identified for each category are summarized in tables, along with the number of studies reporting them and annotations on notable differences between PT and DT. Due to heterogeneity and limited studies on the decision to be informed about additional findings, relevant factors for each category and study heterogeneity are described in the text.

### Critical appraisal

The methodological quality of included studies was assessed by two researchers (E.S.D. and students C.E., J.G., M.Z., ) independently using the Mixed Methods Appraisal Tool (MMAT).[17] Disagreements were resolved by consulting a third researcher (S.P.L.). The MMAT contains two screening questions, as well as five additional questions, specific to study methodology. Each item is evaluated with yes/no/can't tell. The manual advises against calculating an overall score and instead recommends providing detailed information on the evaluation of each criterion. The MMAT version used was revised via a Delphi study to enhance content validity.[18]

## RESULTS

### Study characteristics

A total of 56 articles met the inclusion criteria (see Figure 1). Supplemental Table 3 provides details of the study characteristics. Parental decisions and relevant factors were not the primary focus in all included studies. In three cases there were multiple publications on the same sample – three on joint decision-making between parents and adolescents,[19–21] two on parental perceptions on genome sequencing in their children with cancer,[22,23] and two on family-level experience and drivers regarding DT in children with severe clinical conditions.[3,8] Only new information was included from more recent publications. Two studies

were conducted within the same research project on gNBS, but on different samples and types of decisions.[24,25] Methods of included studies are qualitative (n = 29), quantitative (n = 11), and mixed-method (n = 16). Studies were conducted in 9 locations, most frequently in the US (n = 27) and Canada (n = 12).

The studies reported on parents' decisions in different settings, distinguishing between PT (traditional and extended; n = 13 publications) and DT (n = 41 publications). In two studies, decisions on PT and DT were included.[26,27] Genetic testing was either conducted in clinical practice or research projects. The 41 studies covering decisions on DT primarily included parents of children with autism, hearing loss, developmental delay, cancer, and yet undiagnosed rare conditions or rare genetic diseases. Four studies included rapid genome sequencing decisions made for critically ill children.[5,28–30] One study compared the settings rapid genome sequencing of neonates at NICU and outpatient pediatric patients.[28] In the 13 studies on PT, decisions were pending for children at increased risk due to the presence of diseases such as familial adenomatous polyposis, polycystic kidney disease, or diabetes in the family (traditional PT). On the other hand, PT studies within research projects include decisions made by parent-adolescent dyads without assuming the presence or absence of a specific diagnosis,[19–21] as well as decisions on genomic sequencing of healthy and symptomatic newborns (extended PT).[24,25]

A second differentiation included the type of parents' decisions: 1) in 51 studies *parents' decision and relevant factors (not) to pursue genetic testing* were studied. Of those, 30 studies included only decisions in favor of testing (n = 2 for PT, n = 27 for DT, n = 1 for PT/DT), six studies reported decisions against testing (n = 2 for PT, n = 4 for DT), and 15 studies focused both decision outcomes (n = 6 for PT, n = 9 for DT). Decisions regarding testing were made for various types of genetic tests, including genetic testing for specific variants or exome/ genome analyses. Furthermore, 2) 11 studies on exome or genome

sequencing additionally examined *parents' decisions on choosing specific types of findings*: In a study which resulted in three publications, parent-adolescent dyads decided whether to receive PT findings about preventable/ not preventable, treatable/ not treatable, adult-onset diseases, and carrier status.[19–21] In two studies, parents decided about receiving actionable adult-onset findings from gNBS (i.e. PT) or DT.[25,31] The remaining six studies in DT settings involved deciding about receiving actionable and non-actionable (childhood onset) findings for hearing loss,[11,32] secondary findings in children with rare diseases,[33] incidental findings in cancer patients,[34] and both, secondary and incidental findings in undiagnosed children.[35] See Supplemental Table 3 for details.

**Quality assessment**

A detailed overview of the MMAT criteria to describe study quality[17] is provided in Supplemental Table 4. The majority of studies met all quality criteria, however the relevance of the assessment is limited for the present analysis, as only few publications primarily focused on parental choice.

**Synthesis**

Firstly, factors from relevant studies were extracted and aligned to the model by Smith et al.[8] However, we found that the broader context of DT and PT, in addition to the wider range of decision outcomes (including testing and receiving additional findings), resulted in not all extracted factors being adequately categorized within Smith's framework. Consequently, we introduced two additional categories: "individual circumstances" and "emotional states". The "individual circumstances" category broadens the scope of pragmatic considerations in Smith's model by incorporating aspects such as family history and test setting. These factors have been identified as relevant in studies that have highlighted the influence of external conditions on decision-making and could affect the feasibility, urgency, and relevance of testing.

The category "emotional states" addresses the role of experienced emotions in decision-making, which was a recurring theme in studies focusing on the parental perspective. Ambivalence, confidence, or feelings of being overwhelmed could shape the evaluation process, thus adding a subjective and dynamic dimension to decision-making.

Furthermore, to emphasize the emotional aspects of benefits and risks, we included the term "hopes", while replacing "risks" with "concerns/worries" to more adequately capture the emotional and subjective dimensions of decision-making, with extends beyond objective risks. As illustrated in Figure 2, decision-making involves evaluating benefits and risks, with individual circumstances, values and beliefs influencing the perception and prioritization of these elements. Additionally, emotional states interact with these factors, either reinforcing or complicating the decision-making process.

*[Figure 2 here]*

In the following, the synthesis is structured with the *five categories on the first level:* 1. benefits/hopes (39 studies), 2. concerns/worries (34 studies), 3. values and beliefs (37 studies), 4. individual circumstances (46 studies), and 5. emotional states (27 studies). *On the second level, decision outcomes are reported* (decision to pursue testing and decision to receive additional findings). Table 1 presents the frequency of factor categories in the studies included, separated by decision type.

*[Table 1 here]*

Due to the extensive amount of information, the factors related to the decision to pursue testing are summarized concisely in Table 2, while details, including citations and annotations, are provided in Supplemental Tables 5-9. As most factors overlapped between

DT and PT, we did not separate the settings in the synthesis, but indicated notable differences between DT and PT in Supplemental Tables 5-9.

*[Table 2 here]*

**1. Benefits/hopes**

Perceived benefits and hopes were reported in 37 studies on the decision to pursue testing and in five studies on the decision to receive additional types of findings.

***Decision to pursue testing***

Both parents who chose to test and those who chose not to test reported benefits and hopes. A summary of these benefits and hopes is presented in Table 2. For comprehensive data and references, we advise referring to Supplemental Table 5.

***Decision to receive additional findings***

Parents who decided to receive actionable adult-onset findings for their newborn or child with medical conditions, as well as secondary findings for children with rare diseases rated preparedness and prevention to be beneficial.[25,31,33] Parents perceived potential findings as valuable for their caring role and their own as well as the family's health.[25,31,33] When selecting various PT findings, the primary consideration was perceived improvement in child's health.[20] Wanting to be informed about incidental or secondary findings from DT was related to the hope to receive a diagnosis.[35]

**2. Concerns/worries**

A total of 31 studies reported on parents' concerns and worries about the decision to test, and six studies reported on concerns and worries about the decision to be informed about certain types of findings.

***Decision to pursue testing***

Irrespective of the scenario (PT/DT, parents opting for/against genetic testing), concerns and worries were expressed when deciding about genetic testing, as illustrated in Table 2. The most common concerns reported by parents were emotionally and socially related, such as fear about the potential impact of findings. For details and references, refer to Supplemental Table 6.

***Decision to receive additional findings***

Concerns and worries associated with the decision to receive actionable adult-onset findings in PT of newborns[25] or DT of children with medical conditions[31] included worries about impacts of knowledge on parenting, emotional impacts (anxiety, distress), discrimination (due to political climate or insurances), coping, and a negative effect on the child. Concerns about impacts on parenting style were also reported by parents who decided whether to receive actionable and non-actionable findings in children with hearing loss.[32] Decisions about secondary findings in DT of children with cancer or rare diseases were accompanied by worries concerning the emotional impact, life insurance and potential legal changes in the future,[33] privacy and discrimination concerns.[20]

**3. Values and beliefs**

A total of 34 studies reported on values and beliefs regarding the decision to pursue testing and seven studies regarding the decision to receive additional findings.

***Decision to pursue testing***

Underlying values and beliefs did not differ according to PT or DT setting. Most values were clearly associated with either the decision to test or not to test (Table 2). The most common values associated with testing include the need for control, reducing uncertainty, fulfilling parental responsibility, and (research) altruism. Values and beliefs most frequently associated

with refusing testing include prioritizing the child's autonomy, and specific attitudes, such as general resistance to genetic testing. In one study, parents declined testing their child with hearing loss, viewing deafness as cultural identity rather than an illness.[45] Religion and faith were not clearly linked to a specific decision outcome– some parents who considered their faith decided to test,[5,54] while others had religious reservations towards DNA technology that deterred them from testing.[37] In Smith et al,[8] parents considered responsibility, compassion and understanding of the child, and altruism important, regardless of whether they pursued or declined testing their child. See Supplemental Table 7 for details on citations.

***Decision to receive additional findings***

In a PT study with parent-adolescent dyads, the decision to be informed about different types of findings was underpinned by altruism and information seeking.[20] Parental responsibility and dedication were associated with the decision to be informed about actionable adult-onset findings in both settings: DT of children with medical conditions[31] and PT of newborns.[25] Additionally, a perceived moral obligation was mentioned in DT,[31] while (research) altruism, curiosity, the belief that more information is beneficial, supporting the child's autonomy and recognizing dignity and worth of the child occurred in PT.[25] Declining adult-onset actionable findings in PT were associated with protection of the child's autonomy.[25]

Parents of children with hearing loss who chose to be informed about additional findings (actionable and non-actionable childhood-onset findings), demonstrated greater tolerance of uncertainty than parents who declined to receive additional findings.[11] Curiosity, need for control and reduction of uncertainty and control (e.g. desire not to get any more shocking surprises, desire for certainty), information seeking, and the attitude that it is better to know vs. better not to know played a role for the decision about findings of DT in hearing loss too.[32] Information seeking was also a characteristic of parents associated with the decision to obtain secondary findings in children with rare diseases.[33]

## 4. Individual circumstances

A total of 41 studies named individual circumstances regarding the decision to test or not, and additional nine studies regarding the choice of receiving specific test results. Factors considered include external influences and settings, social environment, and sociodemographic factors.

### *Decision to pursue testing*

Individual circumstances influencing parents' decision to test their child or not to test are illustrated in Table 2. The most frequent factor was parent-physician contact and communication. Factors such as family history, critical child health, and interactions with geneticists or testing recommendations were predominantly associated with the decision to test. Practical barriers, like financial or logistical constraints, were related to the decision not to test. For details and references, refer to Supplemental Table 8.

### *Decision to receive additional findings*

In a PT study with parents' and adolescents' decisions about various categories of findings, parents decided less often to be informed about all conditions (i.e., (non) preventable, (non) treatable, adult-onset conditions, and carrier status) for adolescent daughters than for sons. The likelihood of parents seeking information about non-treatable diseases decreased with increasing adolescent age.[19] The decisions to learn about health conditions were associated with actionability and perceiving the test as a unique opportunity and cost-free.[20] Regarding joint decision-making, parents and adolescents considered the same factors as most relevant to their decision (improving health, helping others, and learning as much as possible).[20] Parents expressed greater concern for privacy and confidentiality and were more interested in learning all possible results compared to adolescents. In this study, 68 of 163 dyads were discordant on one or more choices.[21]

Parents who chose to receive actionable adult-onset findings from newborn genome sequencing did not perceive additional risks. Decliners often reported logistical barriers.[25] Parents in the study either agreed directly, had partially divergent opinions, discussed jointly, or referred to the primary decision-maker, as in other health-related decisions.

Agreement to the disclosure of additional findings from DT for hearing loss, i.e. actionable and non-actionable childhood-onset findings, was related to child's age (lower uptake if infant younger than three months), family size (more likely if two children than one), ethnicity (more likely if child was Australian or New Zealander than other ethnicity) and child's health status.[11] The decision to receive secondary findings from DT for children with rare diseases was related to family history and low perceived risk of abnormal findings.[33]

Parents making decisions about secondary findings from rapid genome sequencing reported they were "not really thinking through" the implications, such as the possibility of sharing genetic information that may be relevant to other family members or the potential impact on other people.[29]

**5. Emotional states**

Information about emotional states were extracted from 24 studies on the decision to pursue testing and from seven studies on the decision to receive additional findings.

***Decision to pursue testing***

Emotional states associated with the decision-making to test are summarized in Table 2 and presented in detail in Supplemental Table 9. Emotions experienced in relation to pursuing testing were confidence and minimal ambivalence. Especially in stressful testing situations, parents commonly experienced emotions such as feeling overwhelmed and ambivalent. Nevertheless, they chose the test. Emotional states associated with refusal of testing included feeling overwhelmed, avoidance, discomfort, and perceived inability to cope with results.

***Decision to receive additional findings***

Across studies in a variety of settings, ambivalence was most frequently reported as an emotional state for at least some parents in relation to the decision to receive information about certain types of findings.[11,25,29,31–34] Sources of ambivalence included weighing up risks and benefits of additional findings and a sense of remissness in not knowing what is knowable.[31] Additionally, parents of children with hearing impairment who chose not to receive additional childhood-onset conditions reported higher levels of anxiety at the time of decision-making compared to parents who sought information about these additional conditions[11] and felt uncomfortable with additional information.[32] Parents who chose to be informed about secondary findings in critically ill children felt grateful for this opportunity.[29] Parents choosing about conditions to learn about their adolescent child in a PT experienced less decisional conflict than their children and were confident in their ability to deal with the findings.[20]

## DISCUSSION

This systematic review examined research on parental decision-making in DT and PT in pediatrics and identified factors that impact parents' decisions. Parents, regardless of their decision on testing, acknowledged benefits but also expressed concerns, particularly regarding emotional and social issues. Parents who chose to test often prioritized benefits over concerns[29,42] or had no concerns at all.[5] Decisions not to test were less studied. The centrality of weighing benefits and concerns in decision-making is also emphasized in the Health Belief Model (HBM),[72] a well-established health psychology theory. It places a focus on cognitive processes driving health-related decisions, suggesting that health behaviors are more likely when individuals perceive high susceptibility to and severity of health risks, as well as benefits and few barriers to action. Decisions to test were associated with values like control, responsibility, and curiosity, while refusal was associated with respecting the child's

autonomy, resistance, or doubts about utility. Circumstances like family history and physician input mostly supported testing, while costs and logistics deterred. Emotional states ranged from feeling uncomfortable to feeling confident to feeling overwhelmed. The range of factors underlines the need to address both cognitive and emotional aspects in genetic counseling, supporting parents in understanding risks and benefits, and also managing emotional challenges. Choosing to receive additional findings was perceived as more complex and challenging than deciding to test, and parents frequently experienced ambivalence. This suggests that such decisions may require more counselling and support when left to parents. Seeking information was associated with actionability, responsibility, curiosity, and tolerance of uncertainty. Factors associated with reluctance included concerns about consequences, increasing adolescent age, and anxiety.

**Extension of the model by Smith et al[8] and implications**

Synthesis of factors relied on the empirical work by Smith et al.[8] Their decision-making framework for pediatric genomic sequencing consists of four primary components that relate to both the family and the child: Underlying values, perceived benefits, perceived risks, and pragmatic considerations. In our synthesis, we assigned extracted factors from relevant studies to these categories. Building on this, we then expanded the model to address the broader context of DT and PT in pediatrics. Accordingly, “pragmatic considerations” were refined into the more encompassing category of “individual circumstances,” and “emotional states” were added as a distinct component. The following sections discuss and summarize the components of the revised model:

The synthesis revealed that benefits/hopes and concerns/worries related to the child, parents and family are often weighed against each other. Parents' values and beliefs regarding child and family, were mostly aligned with the decision outcomes (to test or not, request additional

findings or not). As Smith et al[8] noted, values and beliefs provide a lens through which genetic testing is perceived and shape how benefits and risks are weighed.

Individual circumstances include a broader range of practical and contextual factors, such as costs and contact with physicians (as in Smith et al's model[8]), but also family history, and joint decision-making. Unlike the original framework, where pragmatic considerations were regarded as influenced by values, the expanded category of individual circumstances is viewed as equally fundamental. This is based on the idea that individual circumstances contribute to the decision-making environment. While some aspects of individual circumstances may be influenced by values, others (like family history) can also shape values. Therefore, they are perceived as complementary and positioned on the same hierarchical level. As in the original model, benefits/hopes, risks/worries, values as well as individual circumstances relate to both, the child and the family.

Emotional states refer to parents' actual emotions that arise during decision-making, distinct from anticipated emotions (classified as hopes and worries). They act as an additional layer, influencing the decision beyond the balance of benefits and concerns. They provide a moderating influence that can reinforce or counteract the decision-making process. However, this component needs to be further investigated.

The newly added categories, individual circumstances and emotional states, emphasize the relevance of subjective factors. This is in line with Fuzzy Trace Theory (FTT)[71], which suggests that decisions are often based on gist representations influenced by emotions and experiences rather than verbatim information. FTT highlights the role of values and emotional responses, indicating that decisions in genetic testing contexts are also shaped by subjective interpretations and emotional impacts, not just cognitive risk assessments. The classification of relevant factors for parental decision-making across different contexts,

including DT/PT and decision type, in the light of an empirical framework is a distinctive contribution of this work. It further provides a basis for assessing which factors may affect parents' decisions in less studied, emerging areas of genetic testing, such as gNBS.

**Comparing DT/PT**

Most included studies focused on DT. Comparing PT and DT, both were valued for their potential benefits in treatment and care, but PT was also associated with the advantage of early detection and decision-making about further surveillance. While in DT parents focused on understanding diagnosis and prognosis, PT was motivated by curiosity and interest. Informed family planning and emotionally and socially related concerns were considered in both settings. However, the intensity of concerns might vary, which could not be assessed in this qualitative synthesis. Clinical utility concerns, such as doubts about treatment impact, were specific for DT. In DT higher uptake of genetic testing, more involvement of children, and more automatic than considered decision-making (i.e. little thought, immediately identifying benefit(s) in testing instead of weighing risks and benefits) was found.[29,30] Emotional distress was notably higher in DT, especially with critically ill children.

Key differences between DT, traditional PT, and extended PT like gNBS include a priori risk levels for a genetic disease, symptom presence, and the number of diseases tested. Both DT and traditional PT involve higher a priori risk and either symptoms in the child or within the family, which may explain the similarities in relevant decision-making factors. Notably, only Genetti et al[24] studied the decision not to test in an a priori low-risk setting, while other studies in a priori low-risk settings refer to the decision to be informed about certain findings. Given the limited scope, it is challenging to determine differences in parents' decisions based on a priori risk. When applying the HBM[72] to compare decision-making between DT and traditional PT, it is likely that perceived health threats are highest for DT and still significant for traditional PT (with family history). For expanded forms of PT, such as gNBS, perceived

health threats are assumed to be significantly lower, because an inconspicuous result would be the norm and no symptoms would be present. Given that perceived medical utility is a critical factor, benefits may be particularly prominent in DT for ill children due to potential treatment impacts. The HBM also assumes that cues to action are needed in addition to the cost-benefit analysis and perception of health threat. Cues to action are assumed to be most pressing in DT due to the child's health status. In traditional PT, cues to action would be based on family history. With expanded PT such as gNBS, cues to action are less noticeable. The importance of symptoms as cues to action was also demonstrated in the gNBS study, with lower participation in the well-baby nursery cohort than in the intensive care unit cohort.[24] According to HBM, deciding for genetic testing should be most likely in DT, followed by PT with family history and less likely in extended PT forms such as gNBS. However, the HBM mainly focuses on cognitive evaluations, placing less emphasis on emotional and sociopsychological factors, which our model shows are significant. FTT[71] suggests that the literal a priori risk of disease is not the decisive factor. Instead, the bottom-line understanding of the risk is more relevant. However, gist understanding might be influenced by family history or intense emotions, which may be stronger in parents of sick children, thus, in DT than in PT.

**Limitations**

Research on parental decisions about their child's genetic testing has often focused on those opting for testing, with fewer studies exploring reasons for declining. Reaching parents who decline testing may be challenging as they might be less willing to participate in research. Additionally, biases may arise from research project settings rather than clinical settings and from not considering disease-specific factors. Our analysis simplifies findings by not differentiating diseases and ranking factors by study frequency, not sample size or intensity, due to the qualitative and mixed-methods synthesis.

**Research implications**

Included studies focused more on anticipated emotions, hopes and worries than on experienced emotional states associated with parents' decision-making process. Future research should aim to capture these emotional states more comprehensively to gain deeper insights into their role and impact on parents' decision-making across various genetic testing contexts (DT, traditional PT, expanded PT). Additionally, future studies should explore how disease risk levels influence decision-making, focus more on factors affecting the decision to be informed about specific findings, and investigate dyadic considerations in parental choices. Given most studies are qualitative, there is a need for quantitative research to determine causal relationships and assess the intensity of factors (e.g. concerns in DT/PT).

This systematic review aligns with discussions on ethical challenges in genome-wide testing in children, as outlined by Eichinger et al,[73] covering issues regarding genetic counseling, analysis and interpretation of results, communicating results, and data use. Challenges in parental decision-making overlap with factors in our review, such as financial considerations influencing decisions. Further studies could examine the interplay between ethical issues and decision-making factors in pediatric genetic testing, enriching our understanding of these complex processes.

**Clinical implications**

For genetic counseling, realistically addressing and validating parents' fears and hopes is crucial. While some parents find the decision-making process quick and straightforward, others face ambivalence, and reservations. Additional counseling and decision aids may be helpful for parents with high ambivalence. Particularly, parents reporting high levels of worry or facing stressful situations, such as parents of critically ill children, may require additional emotional support. FTT[71] recommends facilitating the representation of information in simple, but meaningful gist to improve decision-making, evoking emotions and core values without

imposing choices. Tailored counseling should help parents understand complex medical information and avoid hasty or fear-based decisions, focusing on individual needs and emotional states for better gist comprehension.

**Conclusion**

This review identifies and synthesizes emotional, relational, and contextual factors related to parental decisions in pediatric DT and PT, extending the empirical model by Smith et al.[8] The extracted factors were assigned to five categories—1. Benefits/hopes, 2. Worries/concerns, 3. Values and beliefs, 4. Individual circumstances, and 5. Emotional states—highlighting the complexity of decision-making in this context. The inclusion of individual circumstances and emotional states as extensions to the original model emphasized the critical need to consider both the broader personal contexts of families and the emotional climate influencing their decisions. These findings have significant practical implications. Healthcare providers should educate parents on benefits and risks, while considering contextual factors, such as trusting relationships, and recognizing and supporting parents' emotional states. Integrating emotional and cognitive support into genetic counseling may improve decision-making and reduce stress for families. Future research should further explore the role of emotional states in decision-making and their interaction with cognitive evaluations. Additionally, exploring differences between DT, traditional and extended PT, as well as their ethical implications, is important to better understand the impact of family history, numbers of genes tested, and a priori risk on decision-making.

## DATA AVAILABILITY

All relevant data are included in the manuscript files and supplemental materials. Furthermore, the data extracted from the original studies are accessible through the references to the original studies.

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## AUTHOR CONTRIBUTIONS

Conceptualization: B.D., E.S.D., J.M., K.M.S., S.P.L.; Data curation: E.S.D., J.M., K.M.S.; Formal analysis: E.S.D., J.M., S.P.L.; Funding acquisition: B.D., E.W., J.M., K.A.; Investigation: E.S.D.; Methodology: E.S.D., J.M., K.M.S., S.P.L.; Project administration: B.D., E.W., J.M.; Resources: B.D., E.W.; Software: not applicable; Supervision: B.D., J.M.; Validation: E.S.D., S.P.L.; Visualization: E.S.D., J.M., K.M.S.; Writing—original draft: E.S.D.; Writing—reviewing & editing: B.D., E.S.D., E.W., H.B., H.S., J.M., K.A., K.M.S., S.K., S.P., S.P.L.

## ETHICS DECLARATION

Not applicable.

## CONFLICT OF INTEREST

All authors declare no competing interests.

## SUPPLEMENTAL FILE LISTING

Supplemental Table 1. PRISMA 2020 Checklist

Supplemental Table 2. Synthesis Without Meta-analysis (SWiM) reporting items

Supplemental Table 3. Characteristics of included studies

Supplemental Table 4. Critical appraisal of included studies based on the MMAT

Supplementary Search Strategy and Supplemental Tables 5-9

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## FIGURE LEGENDS

**Figure 1.** Study selection process per PRISMA guidelines. [a] Most common exclusion reason during fulltext screening, example: Gal DB, Deuitch N, Lee SSJ, Simon RT, Char DS. Parental Attitudes Toward Clinical Genomic Sequencing in Children With Critical Cardiac Disease. Pediatr Crit Care Med. 2021;22(8):e419-e426. doi:10.1097/PCC.0000000000002669

**Figure 2.** Model of factors for parents' decisions in pediatric genetic testing, including whether to undergo testing and whether to be informed about specific findings. The model is based on the framework proposed by Smith et al.[8] and expanded through a synthesis of reported factors in included studies. It is assumed that values and individual circumstances shape the perception of benefits/hopes and concerns/worries. These components refer to both the child and family. Emotional states experienced by parents during decision-making add an additional layer to the decision-making process.

**Table 1.** Included studies assigned to categories of our extended model based on Smith et al and decision types

| Benefits and hopes | Worries and concerns | Values and beliefs | Individual circumstances | Emotional states |
|---|---|---|---|---|
| **1) Decision to test** | | | | |
| Alam et al 2022,[36] Alderfer et al 2015,[27] Anderson et al 2017,[31] Bon et al 2022,[37] Byrjalsen et al 2018,[34] Chassagne et al 2019,[38] Childerhose et al 2021,[39] Clarke et al 2011,[40] Davis et al 2021,[41] Hanish et al 2018,[42] Harrington et al 2018,[43] Hill et al 2020,[29] Jaitovich Groisman et al 2019,[44] Kaimal et al 2007,[45] Kattentidt-Mouravieva et al 2014,[46] Lee et al 2021,[47] Lesperance et al 2017,[48] Levine et al 2010,[49] Lewis et al 2020,[33] Lucas et al 2022,[50] Malek et al 2017,[22] McConkie-Rosell et al 2023,[51] McCullough et al 2016,[52] Palmer et al 2008,[53] Rosell et al 2016,[35] Sapp et al 2014,[54] Smith et al 2019,[28] Smith et al 2023a,[8] Smith et al 2023b,[3] Tibben et al 2021,[55] Tremblay et al 2018,[56] Tutty et al 2021,[32] Twomey et al 2008,[57] Vears et al 2016,[58] Verberne et al 2022,[59] Wainstein et al 2022,[5] Waldman et al 2022[60] | Alam et al 2022, [36] Alderfer et al 2015,[27] Bon et al 2022,[37] Childerhose et al 2021,[39] Clarke et al 2011,[40] Davis et al 2021,[41] Genetti et al 2019,[24] Hanish et al 2018,[42] Harrington et al 2018,[43] Hill et al 2020,[29] Howard Sharp et al 2020,[61] Jaitovich Groisman et al 2019,[44] Kaimal et al 2007,[45] Kattentidt-Mouravieva et al 2014,[46] Lee et al 2021,[47] Lesperance et al 2017,[48] Levine et al 2010,[49] Lewis et al 2020,[33] Lucas et al 2022,[50] Malek et al 2019,[23] McConkie-Rosell et al 2023,[51] Palmer et al 2008,[53] Rosell et al 2016,[35] Scollon et al 2014, Smith et al 2019,[28] Smith et al 2023a,[8] Smith et al 2023b,[3] Tremblay et al 2018,[56] Tutty et al 2021,[32] Wainstein et al 2022,[5] Waldman et al 2022[60] | Alam et al 2022, [36] Alderfer et al 2015,[27] Anderson et al 2017,[31] Bon et al 2022,[37] Byrjalsen et al 2018,[34] Chassagne et al 2019,[38] Childerhose et al 2021,[39] Clarke et al 2011,[40] Genetti et al 2019,[24] Hill et al 2020,[29] Jaitovich Groisman et al 2019,[44] Kaimal et al 2007,[45] Kattentidt-Mouravieva et al 2014,[46] Lee et al 2021,[47] Lesperance et al 2017,[48] Levine et al 2010,[49] Lewis et al 2020,[33] Li et al 2016,[62] Liang et al 2022,[63] Malek et al 2017,[22] Malek et al 2019,[23] McConkie-Rosell et al 2023,[51] McCullough et al 2016,[52] Palmer et al 2008,[53] Sapp et al 2014,[54] Smith et al 2023a,[8] Smith et al 2023b,[3] Tibben et al 2021,[55] Tutty et al 2021,[32] Twomey et al 2008,[57] Vears et al 2016,[58] Verberne et al 2022,[59] Wainstein et al 2022,[5] Waldman et al 2022[60] | Ahimaz et al 2021,[26] Alderfer et al 2015,[27] Barton et al 2018, Bon et al 2022,[37] Byrjalsen et al 2018,[34] Chassagne et al 2019,[38] Childerhose et al 2021,[39] Christian et al 2018, Clarke et al 2011,[40] Davis et al 2021,[41] Genetti et al 2019,[24] Harrington et al 2018,[43] Hill et al 2020,[29] Howard Sharp et al 2020,[61] Jaitovich Groisman et al 2019,[44] Kaimal et al 2007,[45] Kattentidt-Mouravieva et al 2014,[46] Lee et al 2021,[47] Lernmark et al 2004, Lesperance et al 2017,[48] Levine et al 2010,[49] Lewis et al 2020,[33] Li et al 2016,[62] Liang et al 2022,[63] Lynch et al 2021, McConkie-Rosell et al 2023,[51] McGill et al 2019,[67] Palmer et al 2008,[53] Peterson et al 2022,[69] Rosell et al 2016,[35] Scollon et al 2014,[64] Smith et al 2019,[28] Smith et al 2023a,[8] Smith et al 2023b,[3] Tibben et al 2021,[55] Twomey et al 2008,[57] Vears et al 2016,[58] Verberne et al 2022,[59] Wainstein et al 2022,[5] Waldman et al 2022,[60] Zhao et al 2019[65] | Alam et al 2022,[36] Anderson et al 2017,[31] Bon et al 2022,[37] Byrjalsen et al 2018,[34] Clarke et al 2011,[40] Genetti et al 2019,[24] Hill et al 2020,[29] Howard Sharp et al 2020,[61] Jaitovich Groisman et al 2019,[44] Kaimal et al 2007,[45] Lee et al 2021,[47] Lesperance et al 2017,[48] Levineet al 2010,[49] Li et al 2016,[62] Liang et al 2022,[63] Lucas et al 2022,[50] McConkie-Rosell et al 2023,[51] Sapp et al 2014,[54] Scollon et al 2014,[64] Smith et al 2019,[28] Smith et al 2023,[8] Tutty et al 2021,[32] Twomey et al 2008,[57] Wainstein et al 2022[5] |
| **2) Decision to receive additional findings** | | | | |
| Anderson et al 2017,[31] Lewis et al 2020,[33] Pereira et al 2022,[25] Raghuram Pillai et al 2020,[20] Rosell et al 2016[35] | Anderson et al 2017,[31] Lewis et al 2020,[33] Pereira et al 2022,[25] Raghuram Pillai et al 2020,[20] Rosell et al 2016,[35] Tutty et al 2021[32] | Anderson et al 2017,[31] Downie et al 2020,[11] Hill et al 2020,[29] Lewis et al 2020,[33] Pereira et al 2022,[25] Raghuram Pillai et al 2020,[20] Tutty et al 2021[32] | Berset et al 2023,[21] Byrjalsen et al 2018,[34] Downie et al 2020,[11] Hill et al 2020,[29] Lewis et al 2020,[33] Myers et al 2020,[19] Pereira et al 2022,[25] Raghuram Pillai et al 2020,[20] Rosell et al 2016[35] | Anderson et al 2017,[31] Byrjalsen et al 2018,[34] Downie et al 2020,[11] Hill et al 2020,[29] Lewis et al 2020,[33] Pereira et al 2022,[25] Tutty et al 2021[32] |

**Table 2.** Factors related to parents' decision to test/not to test in pediatric genetic testing.

| Category | Subcategory | Examples | n[a] |
|---|---|---|---|
| **Benefits/ hopes** | Hopes regarding child's health and quality of life | Better treatment options, management of the disease, improved medical care | 24 |
| | Understanding and receiving information | Hopes for better understanding of diagnosis and prognosis (DT[b]), interest, hope to be able to educate child (PT[b]) | 23 |
| | Family benefits | Family planning, learning about family health | 27 |
| | Emotional and coping expectations | Improved preparation and coping, empowerment, sense of completeness, social needs satisfaction | 19 |
| **Concerns/ worries** | Emotional and relational concerns | Fears about potential findings, negative impact on child, parent-related concerns | 28 |
| | Concerns about practical and operational aspects | Discrimination against child, privacy concerns, cost of testing, not right time | 17 |
| | Concerns about medical utility[c] | Doubts about utility, concerns about treatment impact | 4 |
| **Values and beliefs** | Decision to test[d] | Need for control and reduction of uncertainty | 17 |
| | | Parental responsibility | 15 |
| | | (Research) altruism | 13 |
| | | Information seeking and information related beliefs (e.g. knowledge as power) | 8 |
| | | Curiosity | 4 |
| | | Considering religion/ faith/ spirituality | 2 |
| | | Taking advantage of medical/ technological advances | 2 |
| | Decision not to test[d] | Autonomy of the child | 4 |
| | | Specific attitudes, e.g., resistance towards genetic testing, early knowledge about gene status not necessary | 3 |
| | | Lack of interest in research (participation) | 2 |
| | | Protecting the child | 1 |
| | | Concept of illness (cultural concept of deafness) | 1 |
| | | Religious reservations | 1 |
| **Individual circum-stances** | Parent-physician contact | Education, offer, trust | 12 |
| | Joint decision making | Involvement of child, discussion with partner | 11 |
| | Specific test-related considerations | Convenience, low perceived risk of the test | 10 |
| | Family history | Personal experience influencing beliefs; family history or lack thereof as motivator | 8 |
| | Practical and operational barriers | Financial considerations, logistical barriers | 7 |
| | Setting of testing | DT vs. PT, intensive care settings | 7 |
| | Specific medical conditions as triggers | Comorbidities, complaints, severity of disease, undiagnosed condition as triggers for testing | 6 |
| | Socio-demographics | Ethnic differences, child's age | 6 |
| | Knowledge and understanding | Knowledge, misconceptions, professional experience | 5 |
| | Social environment | Lack of social support; family needs and implications | 4 |
| | Geographic location | Rural/underserved vs. urban/well-served areas, city size | 2 |
| **Emotional states** | Experienced emotions | Feeling overwhelmed, stressed, uncomfortable with testing | 8 |
| | Ambivalence and decisional conflict | Mixed feelings, different levels of decisional conflict | 7 |
| | Confidence in coping | Avoidance tendencies, feeling (not) able to cope | 5 |
| | General expectations | High vs. low | 2 |

Categories of our expanded model (Fig. 1), based on Smith et al.'s framework[8], with subcategories and examples for each. For details regarding test setting, decision outcomes, citations, and additional information, we strongly recommend Supplement 6, Tables 1-5. [a] n refers to the number of studies reporting the theme. [b] DT/ PT: diagnostic/ predictive genetic testing. [c] Only reported in studies about DT. [d] Values and beliefs are primarily associated with either the decision to test or not to test.