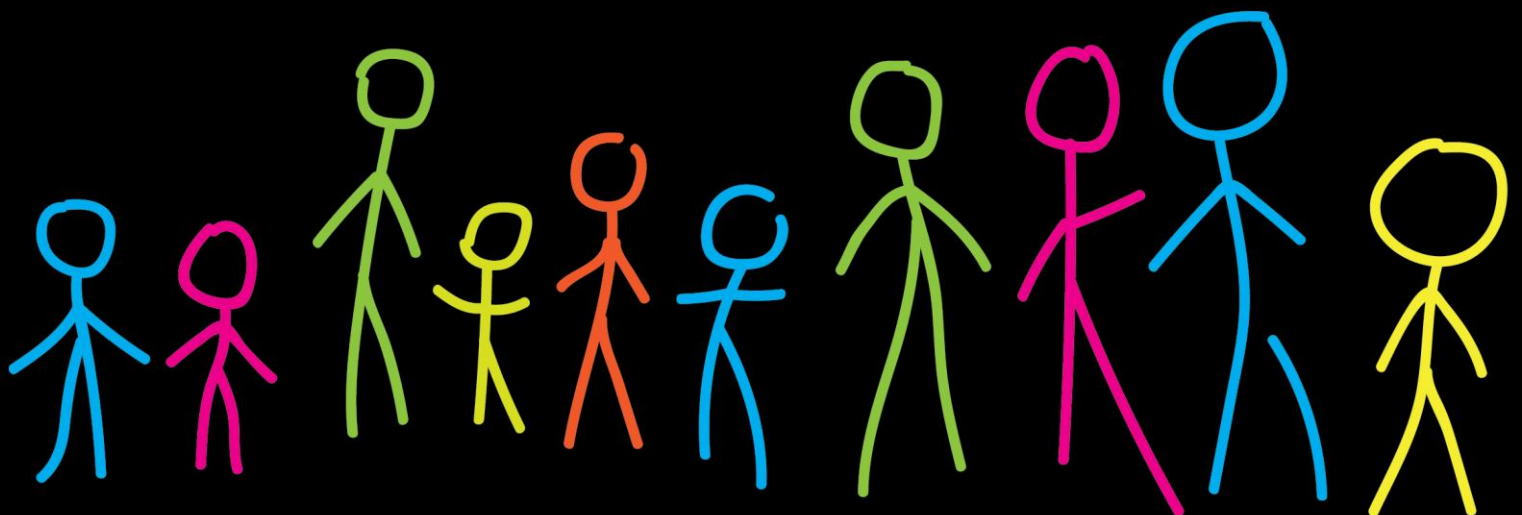




The Rights of Children in Biomedicine:

Challenges posed
by scientific advances
and uncertainties



Kavot Zillén, Jameson Garland,
& Santa Slokenberga

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Executive summary

The Committee on Bioethics of the Council of Europe commissioned this study to identify potential areas of heightened concern for the rights of children that may be unfavorably affected by scientific advances and uncertainties in biomedicine. This report is the result of that study. It provides substantive illustrations of the diversity of problems generated by biomedical developments, including the expanded use of certain biomedical procedures, emerging technologies, and innovative therapies. It also addresses uncertain risks to children through the continuation of longstanding biomedical practices that lack sufficient scientific support. Because considerable legal protections have been developed for biomedical research and continue to be debated in great depth, this report focuses more broadly on biomedicine as a whole. The specific concern addressed here is not about the research process and regulation as such, but rather on how scientific advances and risk-laden practices reach children in biomedicine – whether through health care practices or in other biomedical settings.

Mapping out the areas of concern for this report required not only identifying the technological advances and scientific challenges at stake but contemplating these challenges first and foremost from the perspective of the rights of children as class – formally collectively defined as persons from birth to age 18, unless they have attained majority status. Because a subsequent report will analyze the potential legal frameworks protecting children from the scientific risks and uncertainties identified here, this report identifies the challenges in protecting children relative to those rights that are commonly described in international human rights discourse, with only summary references to specific legal instruments in the report’s conclusions.

The aim of the report is to demonstrate how the scientific risks and uncertainties illustrated here may affect the rights of children from birth through adolescence, in a variety of ways. Chapter 2 surveys differences in childhood development to illustrate why the lack of protection from scientific risks and uncertainty persists, in part because of limited understanding of the developmental differences and vulnerabilities of children at different phases of life. The report then expands on how many interventions may reach children at the earliest stages of their development, such as through assisted reproduction and other interventions *in utero* (Chapter 3) as well as in the field of genetics (Chapter 4). The report then addresses children who have been subjected to high-risk and controversial clinical practices, many of which lack sufficient scientific support regarding their safety. Among those children at risk are sexual or gender minority children (Chapter 5) and children diagnosed with serious physical and mental health needs (Chapter 6). The next chapters address two areas affecting critically ill children where considerable policy debate has taken place, but without sufficient regard to scientific advances and uncertainties, specifically in transplantation (Chapter 7) and end-of-life decisions (Chapter 8).

In the final chapter, the report sets forth numerous rights of children in biomedicine that are currently at stake from scientific advances and uncertainties – not only the right to the highest attainable standard of health but rights protecting their physical and psychological integrity and their privacy and identity, as well as freedom from discrimination. The landscape of these rights is as vast and potentially complex as biomedicine. The report thus concludes that the biomedical controversies surveyed here signal a need for systemic, continuous and multidisciplinary oversight of these issues, as well as for many biomedical interventions that could not be covered here in depth. These matters cannot be left to biomedical expertise alone, but instead require vigilant oversight from human rights authorities and scholars with an understanding of these issues.

Resumé

Le Comité de bioéthique du Conseil de l'Europe a commandé cette étude pour identifier les domaines susceptibles de soulever des préoccupations importantes pour les droits des enfants qui pourraient être affectés par les progrès scientifiques et les incertitudes en biomédecine. Le présent rapport est le fruit de cette étude. Il illustre, sur le fond, la diversité des problèmes engendrés par les évolutions biomédicales, y compris le recours accru à certaines procédures biomédicales, aux technologies émergentes et à des thérapies innovantes. Il aborde également les risques éventuels pour les enfants, liés au maintien dans la durée de pratiques biomédicales dénuées d'un fondement scientifique suffisant. Des protections juridiques considérables ayant été développées pour la recherche biomédicale, et continuant d'être débattues en profondeur, le présent rapport cible plus largement la biomédecine dans son ensemble. Il ne traite pas du processus de recherche et de la réglementation en tant que tels, mais plutôt de la façon dont les progrès scientifiques et des pratiques à risque touchent les enfants dans le domaine biomédical – que ce soit à travers les pratiques en matière de soins de santé ou dans d'autres contextes biomédicaux.

Pour définir les domaines de préoccupations aux fins du présent rapport, il a fallu identifier les progrès technologiques et les défis scientifique en jeux, et ensuite les envisager sous l'angle des droits des enfants en tant que classe – formellement et collectivement définie comme englobant toutes les personnes de la naissance jusqu'à l'âge de 18 ans, sauf majorité plus précoce. Étant donné qu'un prochain rapport analysera les cadres juridiques susceptibles de protéger les enfants contre les risques et incertitudes scientifiques identifiés dans le présent document, notre propos sera d'identifier les défis dans la protection des enfants du point de vue des droits généralement évoqués dans les débats internationaux sur les droits de l'homme, avec seulement en guise de résumé quelques références à des instruments juridiques spécifiques en conclusion de ce rapport.

Ce rapport entend démontrer comment les risques et incertitudes scientifiques cités en exemple peuvent affecter, de diverses manières, les droits des enfants de la naissance à la fin de l'adolescence. Le chapitre 2 aborde les différences de développement dans l'enfance pour illustrer le fait que l'absence de protection contre les risques et incertitudes scientifiques persiste, en partie en raison de la connaissance limitée des différences dans le développement et la vulnérabilité des enfants pendant les différentes phases de la vie. Le rapport s'intéresse ensuite à la manière dont les interventions peuvent toucher les enfants aux stades les plus précoces de leur développement, par exemple dans le domaine de la reproduction assistée et d'autres interventions *in utero* (chapitre 3) et dans celui de la génétique (chapitre 4). Le rapport traite ensuite des enfants exposés à des pratiques cliniques à haut risque et controversées, souvent dans des conditions de sécurité dénuées de garanties scientifiques. Parmi ces enfants à risque, l'on trouve les enfants appartenant à une minorité sexuelle ou de genre (chapitre 5) et ceux chez qui l'on a diagnostiqué des besoins importants en matière de santé physique ou mentale (chapitre 6). Les chapitres suivants couvrent deux domaines concernant des enfants très gravement malades, qui ont fait l'objet de débats politiques importants, mais sans examiner suffisamment les progrès et incertitudes scientifiques, notamment la transplantation (chapitre 7) et les décisions dans les situations de fin de vie (chapitre 8).

Dans le dernier chapitre, le rapport énonce plusieurs droits des enfants dans le domaine biomédical qui sont actuellement mis en jeux par les progrès et incertitudes scientifiques – non seulement le droit de jouir du meilleur état de santé physique et mentale possible, mais aussi le droit à la protection de l'intégrité physique et psychologique, à la protection de la vie privée et de

l'identité, et le droit à la non-discrimination. La situation de ces droits est potentiellement aussi vaste et complexe que la biomédecine. Le rapport conclut donc que les controverses examinées suggèrent la nécessité d'une surveillance structurelle, continue et pluridisciplinaire de ces questions, ainsi que pour de nombreuses interventions biomédicales qui n'ont pas pu être abordées en détail. L'on ne saurait laisser ces questions aux seuls experts en biomédecine, mais elles appellent une surveillance attentive des instances de protection des droits de l'homme et d'universitaires familiarisés avec ces problèmes.



1. Introduction

1.1 The aims of the report

Scientific advances in biomedicine are widely considered the hallmarks of global improvement of the health and quality of life of children. Many biomedical advances, however, come with considerable risks and uncertainties, with the potential to adversely affect children's lives and health. In the context of medical care, for example, when children are patients, they are inherently vulnerable to some degree due to their illness or injury. And yet, their dependence on their parents or guardians amplifies these vulnerabilities, as parents or guardians are expected to make critical care decisions, based on risk assessments, on their children's behalf. These decisions can be especially challenging for parents and children alike, both from a scientific point of view, as well as a legal one. Many risk assessments involve scientifically complex data, a complexity that is often increased when treatments have not been carefully tested and validated according to the best scientific methods. Many interventions may greatly improve children's health but may do so in ways that undermine their rights, which neither parents nor clinicians may fully understand as a matter of law. In the broader field of biomedicine, protections for children may also depend on the beneficence of actors – such as geneticists, fertility specialists, and other developers or providers of biomedical products and services – whose primary professional responsibilities do not include caring for children as their patients. As such, the rights of children in biomedicine must be considered to extend both throughout and beyond clinical practice in intricate ways.

Human rights discourses on the rights of children have long focused on the need for special legal rules to safeguard children as a class. Nevertheless, comprehensive analysis is still greatly needed to understand how scientific advances and uncertainties in biomedicine may affect the varied needs of children, in ways that can adversely impact their rights as individuals. To date, much juridical attention on children in biomedicine has focused on critical subcategories of health care – such as biomedical research and experimentation, as well as the rights of access to essential care and the capacity of children to participate in care decisions. Though extremely important, these issues often eclipse awareness that much scientific risk and uncertainty permeate traditional health care practices, as well as applications of biomedical advances outside clinical settings. Moreover, the focus on the rights of children as a class does not appear to have fully explored the differences among children relative to their ages, specific health needs, and varied interests – all of which may affect the way biomedicine impacts their individual rights. As such, this field of interest – constituted by biomedical advances, innovative therapies, and questionable longstanding clinical practices – represents a vast unexplored territory on the landscape of human rights protections for children in biomedicine.

The Committee on Bioethics of the Council of Europe commissioned this report with the aim of mapping potential areas of heightened concern for the rights of children that may be adversely affected by scientific advances and uncertainties in biomedicine. The aim of this study is to provide substantive illustrations of the diversity of potential challenges to children's rights generated by new technologies, innovative therapies, and uncertain risks from ongoing practices in biomedicine. A subsequent report – also commissioned by the Committee on Bioethics – will independently address the effectiveness of current legal instruments protecting children's rights that may be at stake, both in Europe and under international law. This report, therefore, attempts

to survey scientific advances and uncertainties in biomedicine to prompt discussion of the current framework of children's rights relative to this field of interest. Specifically, the report takes a broad look at different types of biomedical controversies so that future investigations can determine whether human rights frameworks would benefit from a more detailed, comprehensive approach to the rights of children in biomedicine.

Several critical perspectives are needed to promote understanding of the approach taken in this report in assessing the potential impact of biomedical practices on the rights of children. First and foremost, the report should be seen as an effort to emphasize why the diversity of children as a class should be reflected in how their rights are conceptualized so that the effectiveness of these rights in promoting the well-being of children in biomedicine can be better assessed. Second, the report also should be seen as an effort to rethink how risk is defined in a legal context and utilized in biomedical decision-making. This rethinking is particularly important in the context of the inquiry posed by the Committee on Bioethics, which addresses the potential impacts of biomedical advances and uncertainties on the rights of children – in essence, risks that their rights will be violated. Finally, the scope of the report in its examination of biomedical practices must be clarified to emphasize why distinctions between biomedicine, clinical practice, and clinical research may not be fully tenable in identifying where greater risks to children manifest. Increased knowledge about the degree of uncertainty of risks to children that may be common to both clinical research and pediatric clinical practice has challenged the meaningfulness of this distinction, as has the vast overlap of clinical research and practice and deployment of innovative biomedical tools therein, ideally to improve children's health.

1.2 Scientific challenges in biomedicine, pediatric care, and law

1.2.1 Identifying the vulnerabilities and diversity of children as a class

In legal instruments, children are often described collectively as persons from birth to age 18, a class often defined by legal vulnerabilities, requiring special protections under the Convention of the Rights of the Child (CRC).¹ As the Committee on the Rights of the Child has repeatedly cautioned, however, the best interests of the child require taking the individual needs and developmental differences of the child into account.² This view is consistent with biomedical knowledge, with growing research documenting just how different individual children are from each other. The wide age range that demarcates the beginning and end of legal childhood, in fact, encompasses complex and overlapping developmental stages with different vulnerabilities of children at each stage of their childhood. As explained in greater detail in Chapter 2, children at different ages differ in their brain development, their ability to metabolize substances, and critical stages of their growth. Consequently, children may respond to biomedical interventions differently depending on the timing of the intervention. Children also differ according to various medical and hereditary conditions, many of which manifest in childhood. For many children, these conditions prompt more invasive medical interventions than most children will ever experience. Parents for these children may seek scientifically advanced treatment or unproven treatment when no cure is available. For other children, their conditions may lead to many interventions that are highly questionable as medical care, particularly if the conditions are perceived as socially problematic.

¹ See Article 1 of the Convention on the Rights of the Child (adopted 20 November 1989, entered into force 2 September 1990) 1577 UNTS 3.

² See Committee on the Rights of the Child, General comment No. 20 (2016) on the implementation of the rights of the child during adolescence, CRC/C/GC/20. Committee on the Rights of the Child, General comment No. 12 (2009), CRC/C/GC/12, The right of the child to be heard. Committee on the Rights of the Child, General comment No. 7 (2005) Implementing child rights in early childhood, CRC/C/GC/7/Rev.1.

In this light, this report is grounded in the principle that concern for children relative to scientific advances and uncertainties in biomedicine requires anticipating that different interventions will pose different risks to children – both across the child development spectrum and the field of biomedicine. Indeed, while biomedical research has often been considered the locus of the greatest biomedical risk to children, that research has actually documented numerous vulnerabilities of children – the full extent of which is often not well understood. This has prompted caution in clinical practice in how medicines and other interventions should be utilized on children of different ages, albeit without any special corresponding legal protections for such use. Interest in the diversity of children has also spurred biomedical innovations in genetic mapping, the collection of biomedical data, and the development of interventions to preempt future harms to children or even to create healthier children, all in ways that would have been unthinkable generations ago. By default, this intersection of the diversity of biomedical interventions with the diversity of children’s needs and interests signifies that the concerns raised in this study can only be fully addressed by a multifaceted, nuanced approach, one that accommodates the complexity and diversity of potential conflicts that may arise.

1.2.2 Conceptualizing risk in relation to scientific advances, uncertainties, and rights

In seeking to address concerns about the rights of children that may be at stake due to scientific uncertainties about the safety and efficacy of biomedical practices, this report is not limited to analysis of interventions where rights violations have already been firmly established. Though concerns of this regard do feature in this report, the report is premised on the concern that the rate of scientific advances and the high degree of uncertainty inherent in science requires sensitivity to *risks of infringements on rights* as well. In this sense, it is the possibilities of adverse outcomes from biomedical interventions that may have a cascade effect on the rights of children. Cherished rights such as informed consent – whether by the child or by parents in the best interests of their children – may be compromised, as uncertainty of the consequences of many interventions may not be easy to foresee, either for a child’s health or collateral risk to other rights. Infringement may also be possible because many biomedical interventions affect interests that are often broadly described as rights that have not yet been recognized in a biomedical context. This may be especially true when a scientific advance is so novel or complex that special permutations of the rights at stake may need to be officially confirmed.

Consequently, the concept of risk utilized in this report is broader than that which is often deployed in biomedical contexts, where the risk-benefit calculus is often described in terms of physical and sometimes psychological harm to an individual. This narrower conceptualization of risk may arise from the fact that many risk assessments in biomedical research address clinical interventions, most of which are physical, or where the intervention is assessed relative to the promotion of physical health or amelioration of illness or injury. From this point of view, when a person undergoing research will not receive a direct benefit from that research, the principal regulatory concern is that the individual will not be worse off physically or psychologically because of the intervention. To be sure, this limited view of risk in biomedicine is not universal. For example, the Explanatory Report to the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Biomedical Research warns that social risks, such as discrimination and stigmatization, must be taken into account when assessing risk in research.³ The recently updated International Ethical Guidelines for Health-Related Research Involving Humans echoes these concerns, reaffirming as well that while scientific advances may benefit

³ Explanatory Report to the Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research, para 17.

particular communities or groups of individuals, they can also pose risks to communities as well.⁴ For these reasons, as the Guidelines explain, the full range of risks to an individual or a community cannot easily be reduced to a mathematical algorithm.

These considerations favor a broader definition of risk when examining the rights of children that may be at stake from scientific advances and uncertainties associated with biomedical interventions. Many of the rights of children concern matters that do not necessarily involve physical or psychological harm – such as the right to identity, to private life, to receive health-related information, or to be heard – all of which may be adversely affected by biomedical interventions without physically or psychologically harming a child. Even when some physical or psychological benefits accrue to an individual from a biomedical intervention, the treatment may involve a deprivation of liberty or may be carried out in a degrading way. As explained throughout the report, many other core rights related to biomedicine themselves – such as the right to the highest attainable standard of health and the right to informed consent – are directly affected by scientific uncertainty. Thus, the report reflects an assessment that the risks to children in biomedicine should not be narrowly limited to risks of physical and psychological harm.

1.2.3 Locating uncertainty and risk in biomedicine

Historically, biomedical interventions on children occurred mostly through clinical practice, which relied on medical knowledge gathered through centuries of trial and error to provide what was believed to be good care for patients. Backed by clinical experience and presumptions of the beneficence of medical professionals, the primary risk to patients was considered, for centuries, to come from quackery. By the late nineteenth century, the rise of new scientific methods for studying disease and testing innovative methods raised new concerns that experimentation and innovation posed a considerable risk from within medical sciences themselves, requiring regulation. The regulatory paradigm that emerged from these developments supported special regulation for research and experimentation in medical sciences while taking a more deferential approach to clinical practice, which was presumed to be safeguarded by professional standards. The Convention on Human Rights in Biomedicine reflects a European consensus on this paradigm, providing a core framework of human rights that applies to biomedicine in general but a special risk-benefit calculus for children when they are the subject of biomedical research.⁵

In commissioning this report to map the scientific uncertainty and risk that manifest in the field of biomedicine as a whole, the Committee on Bioethics cogently recognizes that questions, at least, should be asked as to whether scientific risk and uncertainty in biomedicine should be most carefully scrutinized in research settings. Indeed, the development of “evidence-based” methods to validate new treatments as safe and effective relative to standard clinical practices has actually led to a growing awareness that many standard clinical practices have never been rigorously validated by sound scientific methods.⁶ Moreover, while legal requirements for testing of pharmaceutical products and high-risk medical devices often require careful testing before they

⁴ Council for International Organizations of Medical Sciences in coordination with the WHO, *International Ethical Guidelines for Health-Related Research Involving Humans* (2016), Guideline 4. CIOMS, <http://www.cioms.ch/ethical-guidelines-2016>, accessed 30 December 2016.

⁵ The full title of the treaty is the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine CETS No.164. Compare Article 4 (Professional standards) with Article 16 (Protection of persons undergoing research) and Article 17 (Protection of persons not able to consent to research).

⁶ Jameson Garland, *On Science, Law, and Medicine: The Case of Gender-‘normalizing’ Interventions on Children Who Are Diagnosed as Different in Sex Development* (Uppsala University 2016) 206–215.

are available for public use,⁷ the same prerequisite does not extend across all health care. For example, the Declaration of Helsinki provides that an unproven intervention may be used in clinical practice, after expert consultation, where “proven interventions do not exist or other known interventions have been ineffective” and where the intervention “offers hope of saving life, re-establishing health or alleviating suffering”.⁸ The Declaration of Helsinki further provides only that such treatment “should” be the subject of research but does not mandate it. Thus, while it is undoubtedly true that children in biomedical research are often subjected to considerable risk,⁹ there are substantial indicators that similar risk, if not greater risk, may occur in clinical practice and other biomedical spheres, where regulatory oversight is lacking.

As this report confirms, a survey of medical and other scientific literature indicates considerable caution about the utility of data that is often used to assert the safety and efficacy of many biomedical interventions. Even in the context of clinical practice, proponents of evidence-based medicine have warned that for most medical interventions, medical journals and treatises remain the primary, public international source of scientific data about the safety and efficacy of diagnoses and treatments. This is so even though this literature is dominated by short-term studies, with small samples of patient data, many of which lack transparency and sound methodology.¹⁰ Poor outcomes are also often unpublished, thus limiting the knowledge and available data regarding actual risk, uncertainty, and harm to all patients, including children.¹¹ Beyond traditional clinical practice, it remains unclear how much objective data exists regarding the safety and efficacy of biomedical interventions offered as elective, commercial services, other than as studied by those who provide those services. For these reasons, this report reflects lessons drawn from evidence-based medicine that even the best available data may only be able to illuminate degrees of uncertainty underlying outcomes from biomedical practices, so that those concerned with such uncertainty can focus on how to manage it and guard against it.¹²

1.3 The parameters and methodology of the report

The directive from the Committee on Bioethics established several parameters for the report by framing the inquiry in terms of scientific challenges and technological advances affecting the health and rights of children, with a particular interest in mapping out areas that may require further investigation of legal instruments for the protection of children. Several consequences from this directive immediately followed in determining the coverage in the report. Because biomedical research is subject to considerable regulation – both in general and specifically regarding pharmaceutical products and medical devices – such research is not the focus of the report. Its output in relationship to scientific risks and uncertainties in biomedicine, however, surfaces throughout the report, particularly for treatments and other biomedical applications and

⁷ In a European context, for example, see Regulation (EC) No 1901/2006 on medicinal products for paediatric use OJ L 378, 27.12.2006, 1–19 and Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices OJ L 331, 7.12.1998, 1–37.

⁸ See WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects, amended by the 64th WMA General Assembly, Fortaleza, Brazil, October 2013, para 37.

⁹ For a thorough summary of the literature and core legal instruments on this subject, especially in a European context, see Katherine Wade, ‘Defining the Threshold of Permissible Risk for Non-Therapeutic Clinical Trials with Children in Europe’ (2016) 24 European Journal of Health Law. For overview of the way scientific risks and benefits are assessed in research, see Lainie Friedman Ross, *Children in Medical Research: Access versus Protection* (Oxford University Press 2006).

¹⁰ Katherine Wade, ‘Defining the Threshold of Permissible Risk for Non-Therapeutic Clinical Trials with Children in Europe’ (2016) 24 European Journal of Health Law. Vinay Prasad and others, ‘A Decade of Reversal: An Analysis of 146 Contradicted Medical Practices’ (2013) 88 Mayo Clinic Proceedings 790.

¹¹ Rafael Dal-Ré, Michael B Bracken and JP Ioannidis, ‘Call to Improve Transparency of Trials of Non-Regulated Interventions’ (2015) 350 BMJ h1323. PA Clavien and Milo Alan Puhan, ‘Biased Reporting in Surgery’ (2014) 101 British Journal of Surgery 591.

¹² Stefan Timmermans and Marc Berg, *The Gold Standard: The Challenge of Evidence-Based Medicine and Standardization in Health Care* (Temple University Press 2010).

interventions that have not been subject to regulations for careful testing before entering clinical practice. Similarly, because the storage and collection of cellular samples and genetic data often intersects with regulation of research and data protection, the regulatory field itself is made highly complex by the overlapping legal orders of the Council of Europe and the European Union in these areas. Thus, while specific advances in genetic testing, sequencing, and editing feature in this report, the broader field of the collection and storage of cellular samples and genetic data is beyond the scope of the report.

Other important areas of concern to biomedicine, such as access to health care generally and the right to the highest attainable health for certain socioeconomic groups, were excluded because these issues do not directly relate to scientific challenges and advances that pose specific risks to children. For the same reasons, the report does not address specific procedures of concern for adults and children alike, such as rights to abortion, prohibitions on compulsory sterilization, and access to experimental care, though they appear in the report where they relate to scientific advances and technological challenges affecting children in biomedicine.

In structuring the report, the broad universally accepted definition of “the child” as an individual from birth to age of 18 is respected for the purpose of the aim of analyzing rights of persons under that age in general. Indeed, because minors, according to this definition, are generally not permitted to consent to treatment or refuse it unconditionally, their rights, in general, are affected by this juridical presumption. Thus, references to “children” in the report without qualification should be read to include all minors, including adolescents, when addressing biomedical and legal interests. For the scientific reasons set forth above, however, this is only the starting point for the analysis that follows. Throughout this report, the focus turns to the different needs and interests of infants, young children, and adolescents and refers to them accordingly where accuracy requires that their status is more carefully delineated.

The legal definition of children, as such, has also merited careful subject selection. Thus, the analysis herein is limited to treatments that are either applied directly to children sometime during the period from birth to age 18 or otherwise designed purposely to affect the life and health of future children, so defined. Issues such as fetal research in general, the selling and transfer of embryos, and stem-cell research are not covered in this report as they neither legally affect the class of children nor do they have a clear or inherent scientific connection to risks to the rights of children. Nevertheless, many biomedical interventions are by design aimed at promoting the health of the future children, including advances in assisted reproductive technology, innovations related to genetics, and treatments *in utero*. These matters are included in this report because they are intended to affect the future child as universally legally defined.

Because this report was designed to map scientific controversies for subsequent legal analysis, the legal inquiry was a limited one. The report evolved from a survey of human rights instruments and other legal documents, so that certain rights could be abstracted as common among them, both as general human rights and rights specifically related to children. Though specific instruments and rights are cited in some instances for illustrative purposes, these references are used solely for illustrations of rights that may be of relevance for future analysis. The identified rights, thus, served as a reference point for selecting particular scientific advances or areas of concern in biomedicine particularly where (1) the lack of evidence supporting safety, benefit or necessity of a biomedical intervention or development has considerable potential to affect the health and physical and mental integrity of the child, or (2) the intervention or development in question raises concerns about risks to the rights of the child, regardless of any risk to the health and physical and mental integrity of the child.

Finally, it must be acknowledged that the work reflects a survey of medical literature, cognizant of its limitations. Thus, these limitations are identified, when relevant, to note whether the data of safety or efficacy is limited, whether full impact of an intervention remains unknown, or when systematic reviews of evidence do not appear to have resolved the controversies in question. Medical treatises were also consulted and compared. Consultation with experts in different fields was also undertaken in select cases to identify particular risks facing children in biomedicine. Because the goal of the report was not to take sides in a particular scientific controversy, the research for this report sought to present an objective analysis based on the quality and transparency of data available.

1.4 The structure and disposition of the report

This report is structured according to the scientific principles set forth so far – that the biomedical needs and interests of children are variable at different stages of child development. Chapter 2, therefore, expands on these themes in detail, by explaining child development from the perspective of biological and cognitive development, focusing on the varied and specialized development of children from birth through adolescence, with illustrations of particular scientific uncertainties and controversies surrounding the impact of biomedicine on children at each stage. As the report concludes, this knowledge is essential to enable non-medical authorities or analysts to readily grasp why a particular biological intervention may be risk-laden for a particular child at a particular age.

Subsequent chapters in the report follow this theme with in-depth analysis. Chapters 3 and 4 reflect how biomedical advances have accelerated various interventions into the earliest stages of childhood development, with the intention of having an impact on producing healthy children. Chapter 3 thus focuses on interventions such as assisted reproduction and those on the future child *in utero*, designed to promote its health after birth. Chapter 4 focuses on biomedical advances in the field of genetics that have spread through and beyond clinical settings as well as broadening the understanding of how biomedicine can be timed in ways to affect future children's health. Chapters 5 and 6 focus on categories of vulnerable children particularly at risk, either because the children are minorities in their own families and society at large or because the diagnostic severity of their medical conditions have resulted in substantial, invasive interventions that are believed by some parents and clinicians to be in their best interests, even though the evidence supporting these interventions as such is often considerably suspect. Chapters 7 and 8 address matters related to transplantation and end-of-life decisions, where considerable policy debate is highly developed and continuous but the scientific uncertainties and risks are not well understood or addressed.

This report concludes that the underlying study should signify the need for a commitment to ongoing monitoring of the biomedical advances and uncertainties identified here, as well as others that were excluded or may have been overlooked. Though many of these questions address highly complex and sensitive matters, the rights of children at stake require multidisciplinary analysis with significant depth – analysis that cannot be left to biomedical experts alone. Rather, the shared interests of authorities and scholars with an understanding of biomedicine and expertise in human rights require collaborative and interactive study for the protection of children in biomedicine in the future.



2. Child development and its relation to medical science

2.1 Introduction

From a biomedical perspective, it has become axiomatic to emphasize that children are not simply small adults. The rationale behind this axiom is a complex, scientific one. While child development is often described in terms of general phases of growth from infancy to adulthood, many aspects of a child's development do not progress in a simple, linear manner. Rather, children develop through a series of overlapping phases, both biologically and chronically, such that any intervention, including a biomedical one, may trigger risk to the development of a child – for example, to its brain, metabolic responses, or overall growth. Moreover, periods of child development described in common parlance are now well understood to be highly generalized periods of time that do not begin or end at the same point in time for each child. For example, though the term “adolescent” is frequently used to refer to older children, the biological definition begins with puberty, the first signs of which may appear for children without disorders at different ages, including before age 10.¹³ As a result, understanding these developmental phases in some detail is critical to fully appreciate the challenges to the rights of children posed by scientific advances and uncertainties relative to the complexities of child development.

This chapter, therefore, summarizes the current biomedical understanding and uncertainties relative to child development, both as to what is known and to what is poorly understood. This chapter is presented before those that follow it because it provides essential context to understand many concerns documented throughout the report. The central concern is not simply that scientific risk and uncertainty may reach children because they are, as a class, unable to protect themselves. Rather, children must be seen as medically and biologically vulnerable at different ages and different phases, raising serious questions as to how and when parents, clinicians, and others in the biomedical field may utilize or encourage interventions on children that could harm them. The purpose of the chapter, therefore, is to highlight these critical developmental stages in physiological terms and, thereafter, in chronological terms, so that the risks to the rights of children in biomedicine during these stages can be more immediately recognized. The chapter then sets forth two of the core rights of children – the right to the highest attainable standard of health and the right to consent and to be heard – both of which can be undermined by scientific uncertainty. As this chapter indicates, the risks associated with these differences are vast, as many treatments that can only be surveyed here could not receive fuller analysis in the report as a whole. The issues raised in this chapter, therefore, should signal a need for comprehensive review of these matters in future works.

2.2 Scientific Background

2.2.1 General developmental principles

One of the strongest biomedical indicators of the complexity of child development is the abundance of clinical pediatric subspecialties required to provide quality care to children. Some of

¹³ See Chapters 2.2.1 and 2.2.2.

these specialties are counterparts to specialties for adults, such as pediatric neurology, cardiology, oncology, and nephrology. These specialties inherently reflect the differences of children relative to adults, such as special diseases and disorders affecting only children or requiring specialized care when a condition occurs in children. Others, such as pediatric endocrinology or genetics, as well as fetal medicine, signify recognition that many conditions affecting adults can be detected and treated in childhood, thus accelerating treatment into childhood, perhaps now more than ever before. On closer examination, the biomedical knowledge that has given rise to these specialties or emerged from them indicates that the need for specialized, diverse care stems from the diverse and complex needs of children at different phases of development.¹⁴

Brain development begins *in utero* as part of a complex neurological process that does not follow a steady, linear progression. The weight of the brain develops rapidly from birth, reaching 80% of adult weight around age two and 90-95% between ages 5 and 6.¹⁵ The architecture of the brain, however, continues to change over time, as billions of neural connections begin to form as the brain remodels itself. Grey matter, where sensory perception, decision-making, and self-control are centered, is believed to peak in growth before adulthood, whereas white matter continues to evolve long after adolescence. Brain development at different stages can be affected by any number of factors, including nutrition, injury, and external stimuli such as stress or music – a condition now theorized as “neuroplasticity”.¹⁶ As a result, interventions at different stages of childhood may seriously impact the brain as a whole or in specific developmental ways, whether the intervention is directed at the brain or aims to treat other parts of the body.

Biochemical processes within the body that are critical to growth are often affected by complex relationships of different organs at different stages of life.¹⁷ The infant’s body, for example, has a greater percentage of water and a lesser percentage of fat at birth, changing as the child grows in infancy, typically followed by muscle development, depending on the child’s mobility and nutritional intake. Renal function, however, accelerates in the first year and peaks in childhood, generally stabilizing to adult levels after puberty. As a result, infants may *metabolize* certain medicines rapidly but may not be able to *excrete* them, such that dosages developed for older children may not only be processed more quickly in infants but remain in their systems and become toxic. In puberty, however, the production of hormones relates to *reproduction* but also to overall *maturation* of the body, in ways that are often not fully understood. For example, the use of oral contraceptives by female minors from puberty through adulthood is now associated with increased risk of breast cancer and cervical cancer but decreased risk of other cancers.¹⁸

¹⁴ Except where noted, the general information in this chapter is drawn from Robert M Kliegman and others, *Nelson Textbook of Pediatrics* (Elsevier Health Sciences 2007). Marilyn J Field and Richard E Behrman (eds), *The Ethical Conduct of Clinical Research Involving Children* (National Academies Press 2004) 62–66. Ralph E Kauffman, ‘Scientific Issues with Biomedical Research Involving Children’ in Michael A Grodin and Leonard H Glantz (eds), *Children as Research Subjects* (Oxford University Press 1994) 29–45. Hannah Batchelor, ‘Paediatric Development: Anatomy, Age, Weight, Body Surface and Stature, Organ Development’ in Daniel Bar-Shalom and Klaus Rose (eds), *Pediatric Formulations: A Roadmap* (Springer 2014) 3–8.

¹⁵ Much of this information has been learned due to research using magnetic resonance imagery, whereas previous knowledge was gained through autopsies and other invasive procedures and x-rays of the brain. See Rhoshel K Lenroot and Jay N Giedd, ‘Brain Development in Children and Adolescents: Insights from Anatomical Magnetic Resonance Imaging’ (2006) 30 *Neuroscience & Biobehavioral Reviews* 718. Today, this research has focused on healthy children. See Deborah P Waber and others, ‘The NIH MRI Study of Normal Brain Development: Performance of a Population Based Sample of Healthy Children Aged 6 to 18 Years on a Neuropsychological Battery’ (2007) 13 *Journal of the International Neuropsychological Society* 729. C Robert Almi and others, ‘The NIH MRI Study of Normal Brain Development (Objective-2): Newborns, Infants, Toddlers, and Preschoolers’ (2007) 35 *Neuroimage* 308.

¹⁶ See Alvaro Pascual-Leone and others, ‘The Plastic Human Brain Cortex’ (2005) 28 *Annual Review of Neuroscience* 377; Krista L Hyde and others, ‘Musical Training Shapes Structural Brain Development’ (2009) 29 *The Journal of neuroscience: the official journal of the Society for Neuroscience* 3019; MR Gunnar, ‘Quality of Early Care and Buffering of Neuroendocrine Stress Reactions: Potential Effects on the Developing Human Brain’ (1998) 27 *Preventive Medicine* 208.

¹⁷ See Kauffman (n 14) 29–30, 38–41.

¹⁸ Oral Contraceptives and Cancer Risk. National Cancer Institute, <https://www.cancer.gov/about-cancer/causes-prevention/risk/hormones/oral-contraceptives-fact-sheet#q3>, accessed 10 November 2016.

Even a broader look at *body composition* and rates of growth in *physiological development* indicates why risks from biomedicine may vary across the class of children. In healthy children, for example, organs assumed to be well developed in childhood, such as the eyes, may react adversely to surgery that is suitable for adults.¹⁹ Some children grow at an atypical or accelerated rate before puberty for a variety of reasons, including genetics, differences in glandular functions, or tumors. Many of these children have long been treated with hormones to stall their growth for “*precocious puberty*”, even though the long-term effects of these drugs on these and other children remain unknown – for example, with potential brain effects for hormones used on young children,²⁰ or harm to fertility for similar treatments to prevent girls from being “too tall”.²¹ In still other children, growth impairments are symptomatic of additional, less visible disorders – such as *phenylketonuria*²² (which prevents processing of a specific amino acid, for which children are screened in infancy to prevent impairments to the heart and brain), or *hypothyroidism*,²³ which can also affect mental and physical growth. Other aspects of growth can be affected by a range of endocrinological, neurological, and genetic disorders. *Progeria*, a rapid aging of the body of children, has no cure,²⁴ neither does *Trisomy 18*, which is a disorder of cell division and inhibits growth.²⁵ Children with these conditions rarely survive into adulthood and likely have different needs and perspectives from those of other children.

From a biomedical perspective, these varied differences in children may appear superficially to raise no need for special legal treatment of children, given that adults too have diverse health needs that may account for different, unpredictable outcomes in response to biomedical interventions. From a developmental perspective, however, it should be clear that children have additional vulnerabilities because their bodies and minds are still forming physiologically – often in ways that are not well understood, if only because research on adults is more common. Concern for children’s rights in biomedicine, therefore, must fully take into account that children are vulnerable in these ways so that different vulnerabilities at different phases of development can be quickly identified when assessing proposed biomedical interventions at different ages.

2.2.2 Developmental periods and their relationship to biomedical risk

The terminology used to differentiate children in their stages of development serves different purposes, many related to the way that the child is assumed to develop socially and behaviorally rather than biologically.²⁶ Many medical classifications of children, for example, focus on “preschool-age” children, an age that by default differs from one jurisdiction to the next as a matter of education policy. The term “adolescent” is often used colloquially to refer to teenagers on general assumptions of when puberty begins, as well as expectations that the children so categorized are likely to engage in particular activities, such as sexual activity or adult-like behaviors. For biomedical risks, however, more scientific precision is required.

¹⁹ See Field and Behrman (n 14) 61.

²⁰ See Jean-Claude Carel and others, ‘Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children’ (2009) 123 *Pediatrics* e752.

²¹ Alison Venn and others, ‘Oestrogen Treatment to Reduce the Adult Height of Tall Girls: Long-Term Effects on Fertility’ (2004) 364 *The Lancet* 1513. AEJ Hendriks and others, ‘Fertility of Tall Girls Treated with High-Dose Estrogen, a Dose-Response Relationship’ (2012) 97 *The Journal of Clinical Endocrinology & Metabolism* 3107.

²² Field and Behrman (n 14) 58.

²³ Kliegman and others (n 14) 1895–1903.

²⁴ Vijay Swahari and Ayumi Nakamura, ‘Speeding up the Clock: The Past, Present and Future of Progeria’ (2016) 58 *Development, growth & differentiation* 116.

²⁵ See Chapter 6.2.1.

²⁶ Except where noted, this section is drawn from Field and Behrman (n 14) 62–66. and Kliegman and others (n 14) 26–55, 532–714.

The *neonatal* period represents the first 28 days following birth, regardless of a child's gestational age. This definition especially accounts for preterm births, as such children may have special needs. It also marks a critical window for all children to determine if they have special disorders or conditions threatening their survival. The World Health Organization (WHO) has emphasized, for example, that nearly half of infant deaths occur during this period, most of these during the first week of life – many of which could be averted by access to antenatal care.²⁷ Equal access to prenatal and antenatal care in Europe, as elsewhere, may be particularly compromised by economic policy, with significant consequences for children's health.²⁸ Low birth weight (LBW), for example, may be caused by a variety of factors (including maternal nutrition and anemia) but without proper care, the neonate may be exposed to a higher risk of death and illnesses, especially during this period.²⁹ Despite advances in neonatal care, much remains to be fully understood to prevent neonatal mortality and injury. Preterm neonates, for example, often lack full cardiovascular, respiratory, and ocular development. Uncertainty in administering the most basic of treatments, such as oxygen, can mean the difference between death and blindness.

Infancy is defined inconsistently in medical works, sometimes capped at age one or two. Pediatric guidelines, as well as human rights guidelines, may favor the broader definition, not only because of the rate of brain development in general, but also because it warrants heightened sensitivity to the way that expression of the child rapidly changes during this period – relative to pain, fear, and general emotional growth. All of the physical, developmental vulnerabilities described in Chapter 2.2.1 remain heightened during this period. Immunology also begins extensively during this period. Children who fail to receive properly timed immunization during this period are likely to become seriously ill from non-fatal conditions spread to them by family members.³⁰

Young children are among the most ambiguously defined class of children, distinguished primarily on the basis that they are no longer infants and have not reached puberty. Thus these children are often separated into “early childhood”, “preschool” categories, or “middle childhood” relative to adolescence. Unlike infants, these children are likely to be socialized but are more mobile and likely to be able to injure themselves or to be infected with illnesses by others outside the home. Access to daycare and school may trigger health concerns, such as infections and lack of immunization, but also concerns about behavioral problems and learning disabilities. The dangers of the accelerated use of medication for psychological conditions during this period of growth are explored in Chapter 6.

Adolescence as a biological matter refers to the period at which puberty begins and ends, though colloquially its endpoint is often presumed to be marked by socio-legal considerations, such as the age of adulthood. Even utilizing this definition, the beginning point is highly variable, depending on how one interprets signs of puberty relative to development and sex characteristics. Feminizing markers, such as breast buds and menstruation, can appear over a highly variable range (median age 12 but ranging from ages 9-16 overall and as young as age 8 in rare cases). In contrast, some masculinizing characteristics appear at age 9, but others appear much later (particularly phenotypes, such as changing voice and facial and body hair). These generalizations for “typical” girls and boys do not account for a variety of differences in many children.³¹ The

²⁷ See WHO, http://www.who.int/pmnch/media/press_materials/fs/fs_newborndhealth_illness/en/, accessed 10 November 2016.

²⁸ See generally, Social Affairs Health and Sustainable Development for the Parliamentary Assembly of the Council of Europe, Ensuring access to healthcare for all children in Europe (2016). Council of Europe, <http://assembly.coe.int/nw/xml/News/News-View-EN.asp?newsid=6377&lang=2&cat=133>, accessed 10 November 2016.

²⁹ Kliegman and others (n 14) 55–59.

³⁰ See WHO, http://www.who.int/immunization/policy/immunization_tables/en/, accessed 12 November 2016.

³¹ For example, as noted above, children with “precocious puberty” have long been subjected to growth suppression therapies, for example, because their accelerated sex development and growth makes their genitals atypically large but shorter in height. The

WHO defines the period as beginning at age 10 and ending at some point after age 18 but cautions that adolescence cannot be rigidly determined by age when examining the individual child.³² Indeed, because of the wide age range involved, most medical and health care authorities urge that the term “adolescence” should be qualified as early, middle and late adolescence to avoid imprecision and misunderstanding of the significance of the term.

Adolescents may be subject to a greater array of challenges, not only due to their changing biology but because their greater social independence may lead them to encounter new forms of risk and conflict with medicolegal norms. As maturity is used as a measure of the weight of consideration given to the child’s views on particular matters such as health care, adolescents may find their maturity tested and cognitive development questioned by medical personnel. At the same time, many adolescents are at risk of sexually transmitted diseases and pregnancy, while others face hardships related to body image, alcohol and tobacco use, and substance abuse. Their need for care for these problems, on the one hand, but with barriers to consent to care, on the other, may pose particular risks to their health. In all of these ways, their inclusion in the class of children underscores the imperfect utility of the broad classification of “childhood”.

2.3 Analysis

2.3.1 The utility of regulation and rights in responding to risk and uncertainty

Empowered by data confirming that children are highly diverse and vulnerable as a class from multiple developmental perspectives, legal authorities could conceivably enact tailored safeguards against scientific advances or ongoing practices that pose uncertainties and risks for children in different ways. Notwithstanding EU regulations for certain medical devices and pharmaceutical products, the competence to provide such safeguards from a legal point of view in Europe generally rests with the national legal orders, particularly for general clinical practice.³³ The Council of Europe respects national legal orders with regard to balancing risks and benefits in health care – both generally and for children – in broad and abstract terms.³⁴ The Convention on Human Rights and Biomedicine, for example, requires that health care must be equitable and of an appropriate quality (Article 3) and that health-related interventions must be carried out in accordance with relevant professional standards (Article 4). The Explanatory Report to the Convention provides that Contracting States are expected to provide care “in the light of scientific progress”, on the one hand, while being “subject to a continuous quality assessment” on the other, but presumes that the general legal rules of the Contracting States share the same fundamental principles in protecting the interests of each patient.³⁵

On the specific question of how national legal orders address scientific advances and uncertainties in biomedicine generally, a comprehensive comparative analysis of the laws of different nations in Europe does not yet appear to have been undertaken. Nevertheless, a survey of different national laws on the regulation of health care standards indicates a wide variety of approaches. Germany, for example, regulates the doctor-patient relationship as a treatment contract, with a presumption that care will be provided according to “recognized medical

broader class of children with intersex conditions or differences in sex development includes variable sex development medically treated as disorders rather than part of the natural diversity of sex development, as explained in Chapter 5.2.

³² For a comprehensive overview, see *Health for the World’s Adolescents: A second chance in the second decade*. WHO, <http://apps.who.int/adolescent/second-decade/>, accessed 12 November 2016.

³³ Santa Slokenberga, *European Legal Perspectives on Health-Related Direct-to-Consumer Genetic Testing* (June 2016) chs 3, 7.

³⁴ Explanatory Report to the Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, paras 25 – 31.

³⁵ *ibid* paras 24, 31.

standards”.³⁶ The evidentiary burden to sustain regulation and prohibitions of treatment falls to the government, whereas patients seeking experimental care may challenge improper care or denials of treatment on evidentiary grounds if medically indicated.³⁷ Spain statutorily requires clinicians to disclose to patients all risks, under normal conditions, based on experience and the state of scientific knowledge.³⁸ It does not otherwise set a scientific, regulatory threshold for valid care, which instead is governed by traditional principles of *lex artis ad hoc*.³⁹ In Belgium, the legal standard of care requires physicians to act in accordance with medical standards and the current state of scientific knowledge, such that liability is often determined based on what the clinician “should have done in a particular case and not what is commonly done”.⁴⁰ Differences such as these can be seen even within regions of Europe that are often thought to have shared values. In Sweden, for example, all medical personnel are required to provide health care according to a standard of “science and carefully tested experience”.⁴¹ In neighboring Finland, the care itself must be of “high quality” but more abstractly “based on evidence”,⁴² whereas Denmark, Iceland, and Norway have even more abstract statutory duties for medical personnel to provide high-quality, conscientious care, without any specific science-based criteria.⁴³ Iceland, however, expressly prohibits medically unnecessary procedures on children.⁴⁴

From both national and international perspectives, it remains unclear at this writing whether a shared regulatory understanding of scientific uncertainty in biomedicine exists. Within the EU, for example, cross-border care may be compensable by an EU citizen’s state of residence if the care is “sufficiently tried and tested by international medical science”, by reference to “existing scientific literature and studies”.⁴⁵ However, current case law from the Court of Justice of the European Union has not yet elaborated on how to evaluate “existing scientific literature and studies”, with their known scientific shortcomings. The Court has also not indicated how studies of variable quality should be weighed – for example, when treatments are new or when no consensus exists about the safety, efficacy, or necessity of established biomedical interventions – on children or any patients. While many national laws may set broad general standards, comprehensive comparative research has not been done in a European context to determine whether these standards are highly detailed and enforced consistently from region to region *within* individual nations or whether many local and regional governments are permitted to promote and enforce their own medical-scientific standards in health care within their jurisdictions.

If, indeed, it is common that regulation is lacking to determine when treatments with uncertain risks and benefits may be utilized in practice, it may be unrealistic to expect that any specific safeguards for children exist or will be developed, especially safeguards specifically designed to protect the diverse vulnerabilities of children, both developmentally and in terms of specific medical conditions. As a result, the rights of children may be inherently at stake because of a lack of these safeguards, particularly the right of each child to receive *the highest attainable standard of*

³⁶ The German Civil Code, § 603a.

³⁷ See Garland (n 6) 581.

³⁸ Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica, Artículo 10.1(c).

³⁹ Miquel Marin-Casals and Josep Sole, ‘Medical Liability in Spain’ in Bernhard A Koch and Ewa Baginska (eds), *Medical Liability in Europe: A Comparison of Selected Jurisdictions* (Walter de Gruyter 2011) 462.

⁴⁰ Hermann Nys, ‘Medical Liability in Belgium’ in Bernhard A Koch and Ewa Baginska (eds), *Medical Liability in Europe: A Comparison of Selected Jurisdictions* (Walter de Gruyter 2011) 462.

⁴¹ The Patient Safety Act (2010:659), chapter 6, section 1. (transl. by J. Garland).

⁴² The Health and Medical Services Act, 30.12.2010/1326, § 8 (2016).

⁴³ For Denmark, see Law on the Authorization of Health Care Personnel, LBK nr 877 af 04/08/2011, § 17. For Iceland, see Healthcare Practitioners Act No. 34/2012, Article 13, and for Norway, see Law on Health Care Personnel, (Lov 2. juli 1999 nr. 64 om helsepersonell m.v.), § 4.

⁴⁴ Patients’ Rights Act, No. 74/1997 (Iceland), Article 27.

⁴⁵ See case C-157/99 *B.S.M. Geraets-Smits v Stichting Ziekenfonds VGZ and H.T.M. Peerbooms v Stichting CZ Groep Zorgverzekeringen* ECLI:EU:C:2001:404, paras 97-98.

health, as well as the *right to be heard*, both of which may increase in importance in light of interventions that risk infringement of numerous other rights identified throughout this report.

2.3.2 Scientific uncertainty and the right to the highest attainable standard of health

The right to the highest attainable standard of health surfaces throughout discourse on the rights of children, as it does in this report. Advances in biomedicine for improving the quality of care are appropriately seen as central to that right. As explained in Chapter 1.2, however, biomedicine has sharpened the understanding of how weak much validation of current practice is, with resources devoted only to testing some new, unproven treatments before they enter care. The challenge of determining whether the right to the highest attainable standard of health has been fulfilled in the midst of scientific uncertainty can be daunting, especially to the extent that it is often difficult to distinguish unproven new treatments from unproven practice standards – largely on the basis of clinical experience, professional judgment, and limited evidence.

For children at different stages of development, these risks can, in fact, be particularly present when clinicians attempt to resolve scientific uncertainties in clinical practice by combining practice with clinical research. This problem was illustrated by the recent controversy over “research within the standard of care” of how much oxygen to provide neonates. In the 1950s and 1960s, premature infants were increasingly given high doses of oxygen to prevent death in standard care, which led to ocular disease and blindness.⁴⁶ For decades, a standard but flexible dose has been difficult to establish; indeed no Europe-wide standard existed until recently, other than to monitor and continually adjust levels of oxygen and surfactants to keep neonates alive while reducing risk of ocular injury. This led to clinical research on more than 1500 neonates in the US, which was proposed to their parents as adjustments of oxygen given to the neonates within the range of standard care. In fact, the accepted range of oxygenation at the time of the trial had been narrowed by clinical experience to a low level of 85%, where death was likely, to a high level of 95%, risking ocular disease. The SUPPORT trial, as it was known, randomly assigned neonates to two groups divided within this range, with some given 91-95% oxygen levels and some given 85-89%. Of the children enrolled in the study, 130 in the low oxygen group died, which, the study authors concluded, indicated an “an increase in mortality” due to restricted oxygenation.⁴⁷ After the SUPPORT trial, European standards, which previously had no lower limit, were raised to 90% oxygen levels as a baseline, while US standards have closed in on that recommendation.⁴⁸ Though considerable uncertainty remains as to whether the trial caused the observed harms in the children, questions remain about whether the trial was truly “within” the standard of care and whether parents should have understood the modification of it.

Similarly complex risk assessments can be illustrated in the field of immunology for older infants and young children, such as the controversial pertussis trials in Sweden and Italy to test vaccines as standard care in different countries, developed in the US, Japan, and Canada. In the US, a randomized control trial testing “no vaccination” against the US-approved vaccine would have been considered malpractice – given that vaccination was the standard of care in the US, and a child might contract pertussis without it and possibly die.⁴⁹ Sweden and Italy, however, had

⁴⁶ Garland (n 6) 376–377.

⁴⁷ Sabrina Tavernise, ‘Study of Babies Did Not Disclose Risks, US Finds’ [2013] *The New York Times* 26. Waldemar A Carlo and others, ‘Target Ranges of Oxygen Saturation in Extremely Preterm Infants’ (2010) 362 *The New England journal of medicine* 1959.

⁴⁸ Clyde J Wright and Ola D Saugstad, ‘OHRP and SUPPORT: Lessons in Balancing Safety and Improving the Way We Care for Patients’ (2013) 163 *The Journal of Pediatrics* 1495. Ola Didrik Saugstad and Dagfinn Aune, ‘Optimal Oxygenation of Extremely Low Birth Weight Infants: A Meta-Analysis and Systematic Review of the Oxygen Saturation Target Studies’ (2014) 105 *Neonatology* 55. Lisa M Askie, ‘Optimal Oxygen Saturations in Preterm Infants: A Moving Target’ (2013) 25 *Current Opinion in Pediatrics* 188.

⁴⁹ Warren E Leary, ‘Critics Question Ethics of U.S.-Sponsored Vaccine Tests in Italy and Sweden’ *N.Y. Times*, Mar. 13, 1994, p. 26.

abandoned the vaccine because of concerns about its safety and efficacy, and thus, could serve as sites with “control groups” of unvaccinated children for comparative data.⁵⁰ For all of the vaccines tested, a minority of the children experienced convulsions, collapse, vomiting, infections, and other adverse reactions, though the adverse reactions for the US vaccine were so substantial that attending nurses could identify more than half of the children receiving it, despite the trial blinding them from knowing which child received which vaccine.⁵¹ The US vaccine proved inferior to the rival vaccines, which became standard care in many parts of Europe, though resistance to those vaccines and concerns about cross-border infections care are now requiring testing of new vaccines against standard care on other infants.⁵²

As subsequent chapters will show, children at different stages of life are subjected to a substantial array of biomedical interventions in standard care and in research that overlaps with it. For the right to the highest attainable standard of health, however, even marginal uncertainties caused by questionable studies about standard care can have catastrophic effects on children. As the recent controversy over claims of autism caused by vaccines has shown, a single study – one that was not properly vetted by the medical journal that published it and retracted only after years of research invalidated it – deterred parents from seeking vaccines that did not, in fact, cause autism. That publication has been notably described as “the most damaging medical hoax of the last 100 years”.⁵³ Incidents such as these, therefore, signify that scientific data about the quality of care for children within standards of care require special scrutiny. The medical literature today currently forecasts the imminent expansions of nanotechnology and gene therapy into clinical practice, each with its own considerable uncertainties, demonstrating how the boundaries between standard care and biomedical inventions continue to blur.⁵⁴ Thus, to ensure that children receive the highest attainable standard of health care, systemic oversight may be needed to ensure that the production of biomedical knowledge is carefully vetted to ensure that biomedical interventions on children do not compromise their safety and quality of life.

2.3.3 Scientific uncertainty and the right to consent or to be heard

The CRC requires all signatories to assure that children have the right to express their views on matters affecting them and that their views are given weight in accordance with the child’s maturity and age.⁵⁵ The science regarding the cognitive development of children can, thus, play a critical role in the rights of an individual child, as a theoretical lack of such development is often used to argue against deference to the wishes of the child. This may occur with regard to the right to consent or refuse treatment (where mature children may consent) or in determinations of the

⁵⁰ Lennart Gustafsson and others, ‘A Controlled Trial of a Two-Component Acellular, a Five-Component Acellular, and a Whole-Cell Pertussis Vaccine’ (1996) 334 *New England Journal of Medicine* 349. Patrick Olin and others, ‘Randomised Controlled Trial of Two-Component, Three-Component, and Five-Component Acellular Pertussis Vaccines Compared with Whole-Cell Pertussis Vaccine’ (1997) 350 *The Lancet* 1569.

⁵¹ Gustafsson and others (n 50) 353.

⁵² Hans Hallander and others, ‘Antibody Responses to Bordetella Pertussis Fim2 or Fim3 Following Immunization with a Whole-Cell, Two-Component, or Five-Component Acellular Pertussis Vaccine and Following Pertussis Disease in Children in Sweden in 1997 and 2007’ (2014) 21 *Clinical and Vaccine Immunology* 165. M van Gent and others, ‘Analysis of Bordetella Pertussis Clinical Isolates Circulating in European Countries during the Period 1998–2012’ (2014) 34 *European Journal of Clinical Microbiology & Infectious Diseases* 821. Ingrid Torjesen, ‘Proteins Targeted by Pertussis Vaccine Are Mutating Unusually Quickly, Study Finds’ (2014) 349 *BMJ* g7850.

⁵³ Dennis K Flaherty, ‘The Vaccine-Autism Connection: A Public Health Crisis Caused by Unethical Medical Practices and Fraudulent Science’ (2011) 45 *Annals of Pharmacotherapy* 1302. Trisha Greenhalgh, ‘Why Did the Lancet Take so Long?’ (2010) 340 *BMJ* c644. (describing the damage done once it was published, “the ghastly social drama of the demon vaccine took on a life of its own”). Mark B Pepys, ‘Science and Serendipity’ (2007) 7 *Clinical Medicine* 562.

⁵⁴ Rachael M Crist and others, ‘Common Pitfalls in Nanotechnology: Lessons Learned from NCI’s Nanotechnology Characterization Laboratory’ (2013) 5 *Integrative Biology* 66. Mary C Machado and others, ‘Nanotechnology: Pediatric Applications’ (2010) 67 *Pediatric research* 500. For background materials on gene replacement therapy, see National Institutes of Health, What is gene therapy? U.S. National Library of Medicine, <https://ghr.nlm.nih.gov/primer/therapy/genetherapy>, accessed 14 November 2016.

⁵⁵ Convention on the Rights of the Child, 1577 UNTS 3, Article 12.

weight given to the child's express wishes.⁵⁶ While countless medical conditions warrant parents and clinicians making medical decisions in the best interests of a child, the notion that scientific uncertainty can determine the scope of the right of a child to consent or be heard is a profound one, especially where the recognition of the legal right is heavily determined by biomedical expertise.

Primary evidentiary support in the medical literature for the claim that most minors are not mature enough to make serious medical decisions is often drawn from neuroscience and other studies, which purport to show that individuals under age 21 downplay long-term consequences and the risks of their decisions (even though that factor might also militate against young adults over 18 consenting to their own health care).⁵⁷ Studies such as these, however, are rarely based on clinical analysis of children's consent in a health care context, where the ability to understand risks might vary depending on condition-specific diagnoses and treatments. For example, a child who is sexually active and contracts a sexually transmitted disease may be legally able to consent to sex with another minor and have a need for care, but may face difficulties regarding consent to receiving such care.

In the health care setting, significant data shows that the presumption that parents and physicians are better positioned to determine treatment options is often not warranted. For children facing end-of-life decisions, research shows that children are sometimes more comfortable discussing treatment generally than physicians and parents are in discussing that information with a child.⁵⁸ In cases of life-threatening illness, the literature also indicates that parental stress and trauma may not only impair parental judgment but may undermine the long-term health of a child.⁵⁹ In these cases, many minors with shorter life expectancy may have more relevant experience to their own conditions, experience that may even be incomparable to that of adults, as these children may have very mature views of their own lives or imminent mortality. Perhaps of most importance, research on treatment of children with chronic conditions shows that clinicians' abilities to know *which* information parents need and *how* to provide that information do not often correspond to parents' views of *what* they or their children want or need to know.⁶⁰

Moreover, children who undergo extensive treatment, as for cancer, have first-hand experience with the treatment that parents and physicians have never endured and are in a better position to know if they want to continue it, particularly if the illness recurs. In this regard, it is now scientifically accepted that pain in children is underappreciated, as pain cannot be predicted or measured with accuracy by physicians and may be highly traumatic to children who survive aggressive treatment.⁶¹ Substantial evidence indicates that pain from treatment can have damaging long-term effects on survivors,⁶² which parents, who may focus only on survival

⁵⁶ This section was adapted from Garland (n 6) 316–319.

⁵⁷ Laurence Steinberg, 'Does Recent Research on Adolescent Brain Development Inform the Mature Minor Doctrine?' (2013) 38 *Journal of Medicine and Philosophy* 256.

⁵⁸ Rebecca S Berger, 'Including Adolescents and Young Adults in Decisions at the End-of-Life' (2012) 5 *Journal of Nursing Res* 12, 14.

⁵⁹ Kristen M Rabineau, P Alex Mabe and Roger A Vega, 'Parenting Stress in Pediatric Oncology Populations' (2008) 30 *Journal of Pediatric Hematology/Oncology* 358. Christina JM Colletti and others, 'The Relationship of Parental Overprotection, Perceived Vulnerability, and Parenting Stress to Behavioral, Emotional, and Social Adjustment in Children with Cancer' (2008) 51 *Pediatric Blood & Cancer* 269.

⁶⁰ Tove Lundberg and others, 'From Knowing Nothing to Knowing What, How and Now: Parents' Experiences of Caring for Their Children With Congenital Adrenal Hyperplasia' (2016) *Journal of Pediatric Psychology* 1.

⁶¹ Richard Howard, 'Current Status of Pain Management in Children' (2003) 290 *JAMA* 2464.

⁶² Robert M Kennedy, Janet Luhmann and William T Zempsky, 'Clinical Implications of Unmanaged Needle-Insertion Pain and Distress in Children' (2008) 122 *Pediatrics* S130. Failure, in fact, to manage preliminary pain can make long-term pain worse. *See* Michelle A Fortier and others, 'Attitudes Regarding Analgesic Use and Pain Expression in Parents of Children with Cancer' (2012) 34 *Journal of Pediatric Hematology/Oncology* 257.

outcomes, may not be able to assess.⁶³ This literature merits strong consideration that pain management should presumptively be developed in consultation with children.

In this light, significant questions remain about assumptions that medical personnel are qualified to make maturity assessments, both on medical grounds – without objective criteria – but also on legal grounds, about the rights of the child.⁶⁴ Errors made in such assessments could harm children in multiple ways – for example, excluding parents when their input is needed in favor of an assumption that the child is mature enough to decide, or excluding the child’s input when it should be dispositive. As will be explored in Chapter 6, the quality of science in the field of psychiatry and psychology is now subject to intense scrutiny, challenging the assumption that any single particular psychiatrist or psychologist, by virtue of training, can always soundly determine a child’s cognitive development and maturity. A clinician without such training is even less likely to be able to make quality maturity assessments in day-to-day clinical practice. Until the science of maturity assessments is confirmed, greater research is needed to determine when such assessments ensure or undermine the right of the child to be heard or consent from case to case.

2.4 Summary of the rights at stake

Advances in biomedicine have unquestionably improved scientific knowledge about the biological complexities of children and risks to their health. They have also, however, exposed scientific gaps in standard care, as well as gaps in knowledge about how biomedical interventions will affect children’s health and their rights. Biomedical interventions with unpredictable or unnecessary risks threaten to undermine the right of children to *the highest attainable standard of health*, whereas uncertainty regarding the science of cognitive development and the ability of health care professionals to assess a child’s maturity can threaten *the right of the child to be heard*, at the very least. Both of these concerns signal the need for more than a survey of current scientific challenges to children’s rights. Indeed, many challenges, as emphasized throughout the report, are far too numerous to be studied in detail here. Rather, the general relationship of child development to biomedical science and interventions warrants comprehensive review and ongoing monitoring to ensure that the core rights of children in biomedicine are protected.

Scientific challenge/procedure	Rights at stake
Scientific gaps in standard care in relation to child development	<ul style="list-style-type: none"> ● Right to the highest attainable standard of health
Scientific gaps in standard care in uncertainty regarding cognitive development	<ul style="list-style-type: none"> ● Right of the child to participate in decisions affecting the child ● Right to consent

⁶³ Michelle A Fortier and others, ‘Pain Management at Home in Children with Cancer: A Daily Diary Study’ (2014) 61 *Pediatric blood & cancer* 1029.

⁶⁴ It is well settled that competence assessments become less arbitrary when medical and legal criteria are provided to practitioners. See Paul S Appelbaum, ‘Assessment of Patients’ Competence to Consent to Treatment’ (2007) *NEMJ* 1834.



3. Interventions at the earliest stage of human development that affect the future child

3.1 Introduction

One of the most innovative shifts in biomedicine in relation to children in the last half-century is the accelerated use of new technologies at the earliest stages of human development to create healthy offspring. The most widely recognized way in which this has been done is through the use of assisted reproductive technology (ART), which traditionally has been used to help persons with difficulties conceiving children. Today, ART has begun to focus on ways to ensure that children are born healthy and to correct genetic disorders in the future child through embryo modification. Increasingly, procedures that were once performed on older children are also being performed *in utero*, with the aim of preventing different birth anomalies in future children. Both of these developments represent a heightened use of technology, innovation, and experimentation in more ways than ever before to affect the health of future children.

The procedures in this chapter are linked for two primary reasons. First and foremost, the practices examined affect the future child when its rights are protected under international human rights law but are utilized prenatally. Thus, the health of the future child is one aim of the use of these technologies even though the child may not be considered to be a legally recognized patient or the sole patient. For ART, the prospective parents are the patients, whereas, for procedures *in utero*, the child-bearer is the patient along with the future child. In these cases, the interests of the parents may take precedence over the child's, particularly if one factor in the decision to consent to the procedure is to exercise their rights to decide whether to terminate the pregnancy or to proceed with birth in the hope that the technologies will fulfill the promise of producing a healthy child. This chapter, therefore, focuses on the scientific uncertainties surrounding these procedures, particularly from the perspective of the health and wellbeing of the future child, with risks that may manifest only after the child is born.⁶⁵ They also may involve interests of the child that extend beyond physical health, including their rights related to health information or their right to identity, autonomy, and freedom from discrimination.

3.2 Assisted reproductive technology (ART)

3.2.1 Scientific background

Assisted reproductive technology is used to facilitate successful pregnancy and childbirth, through the handling of gametes (sperm or ova), often with fertilization outside the human body. Technologies, such as *in vitro* fertilization (IVF) and assisted insemination are used worldwide in

⁶⁵ As explained in Chapter 1.3, the future child in this report only refers to those children from birth, as consistent with the Convention on the Rights of the Child. The analysis in this chapter solely focuses on the concerns of the born child. It does not address any implications of the moral or legal status of embryos or fetuses, which are beyond the scope of the report.

order to help individuals and couples to conceive a child.⁶⁶ According to the European Society of Human Reproduction and Embryology more than 6.5 million children have been conceived through IVF worldwide since 1978.⁶⁷ As such, ART may be perceived as so well-established that it is no longer considered a scientific advance. Indeed, on the whole, the biomedical literature does not provide evidence to challenge the assumption that many healthy children have been produced through ART and may be safe as a means of procreation.

Nevertheless, even among researchers who are engaged in and support ART, the medical literature reveals significant concern about whether ART poses special risks to the health or other interests of children. These concerns may be categorized as follows.

- ❖ *The science of creating healthy children with ART:* Much of the outcome data regarding the health of children born from ART remains problematic because of a lack of long-term data and follow-up on children through their lives. Sufficient evidence exists, however, to caution that children born from ART may be more likely to be preterm or suffer from low birth weight, as well as experience other physiological problems, such as impaired growth. Some of these risks may be more likely to manifest when ART utilizes frozen oocytes or embryos.⁶⁸ Significant research on the use of gonadotropin (GnRH) analogues on older women to stimulate ovary production has raised alarm that those substances, used at such an early stage of child development, may have an effect on the health of the child.⁶⁹ A recent study conducted on young adult men born after IVF using intracytoplasmic sperm injection (ICSI)⁷⁰ indicates that their sperm count may be significantly lower than the norm, warranting more inquiry into the techniques used in ART.⁷¹ Genetic research also indicates that stress on the embryo during the ART process may affect its development.⁷² These concerns clearly indicate the need for more research with careful controls and systematic review of long-term data but are sufficient to at least require consideration of the possibility that certain methods may affect the health of the future child.

- ❖ *Techniques to detect potentially adverse medical conditions:* Preimplantation genetic diagnosis (PGD) is often used to detect genetic diseases in embryos created through IVF before implantation and pregnancy to maximize the chance of a healthy child being born without a genetic

⁶⁶ In some cases ART requires the use of reproductive resources from a third party (third party assisted ART), such as sperm or egg donation (donor gametes), or a surrogate or gestational carrier. In contrast to traditional surrogacy, the gestational surrogate does not provide her own genetic material and thus has no genetic link to the child born. Gestational carrier arrangements might therefore not be as legally controversial from a child's rights perspective, as traditional surrogacy.

⁶⁷ Third-party Reproduction, A Guide for Patients, 2012, 3. American society for reproductive medicine, https://www.asrm.org/uploadedFiles/ASRM_Content/Resources/Patient_Resources/Fact_Sheets_and_Info_Booklets/thirdparty.pdf, accessed 19 November 2016.

⁶⁸ Abha Maheshwari, Edwin Amalraj Raja and Siladitya Bhattacharya, 'Obstetric and Perinatal Outcomes after Either Fresh or Thawed Frozen Embryo Transfer: An Analysis of 112,432 Singleton Pregnancies Recorded in the Human Fertilisation and Embryology Authority Anonymized Dataset' (2016) 106 *Fertility and Sterility*. Shuang Jing and others, 'Obstetric and Neonatal Outcomes in Blastocyst-Stage Biopsy with Frozen Embryo Transfer and Cleavage-Stage Biopsy with Fresh Embryo Transfer after Preimplantation Genetic Diagnosis/screening' [2016] *Fertility and sterility*. Catrin E Argyle, Joyce C Harper and Melanie C Davies, 'Oocyte Cryopreservation: Where Are We Now?' [2016] *Human reproduction update* dmw007.

⁶⁹ Adam H Balen and others, 'The Management of Anovulatory Infertility in Women with Polycystic Ovary Syndrome: An Analysis of the Evidence to Support the Development of Global WHO Guidance' (2016) 22 *Human Reproduction Update* 687. Stefano Palomba and others, 'Pregnancy Complications in Women with Polycystic Ovary Syndrome' (2015) 21 *Human Reproduction Update* 575. Tim Savage and others, 'Ovarian Stimulation Leads to Shorter Stature in Childhood' [2012] *Human reproduction* des249. Margarida Avo Santos, Ewart W Kuijk and Nick S Macklon, 'The Impact of Ovarian Stimulation for IVF on the Developing Embryo' (2010) 139 *Reproduction* 23.

⁷⁰ In situations where the number or quality of sperm is insufficient to allow fertilization in IVF treatment, individual sperm may be injected into eggs by means of ICIS. The injection may be performed with ejaculated sperm or with sperm retrieved surgically from man's testicles.

⁷¹ F Belva and others, 'Semen Quality of Young Adult ICSI Offspring: The First Results' [2016] *Human Reproduction*.

⁷² Gael LM Cagnone and Marc-André Sirard, 'The Embryonic Stress Response to in Vitro Culture: Insight from Genomic Analysis' [2016] *Reproduction* REP.

disease or disorder. The embryos are tested for certain inherited conditions or chromosome abnormalities, such as cystic fibrosis, spinal muscular atrophy, and Huntington's disease. The process involves the removal of a cell from an embryo, fertilized outside the woman's body (using IVF), to test it for a specific genetic condition (embryo biopsy) after it has grown in the laboratory for two to six days.⁷³ Thereafter, the embryo cells are tested for genetic conditions. Only those embryos with normal chromosome structures that do not carry the mutation(s) related to a particular disease are selected for transfer to the mother's womb during IVF treatment. It also enables the embryos to be screened for other conditions, such as the susceptibility to cancer and late onset diseases (diseases that develop later in life), such as Alzheimer's disease.⁷⁴

The removal of cellular samples from the future child while in their embryonic state has yet to be confirmed to be low-risk and harm-free to the child. Currently, the quality of scientific studies is low but indicates that children born after having cells removed from PGD may have a higher rate preterm birth and other neonatal risks, with uncertainty about links to congenital anomalies, regardless of the age or condition of the mother.⁷⁵ As with studies on ART in general, much of the controversy persists because of the lack of long-term data and carefully controlled studies that focus on the health of the child. Instead, the medical literature tends to be based comparisons between children born in the general population without the questioned intervention to determine if they suffer from congenital anomalies or other impairments. This data, however, remains highly problematic in answering the question of whether the technology itself causes the harm. Anomalies in the general population may come from inherited conditions in natural childbirth, but anomalies due to PGD – much like freezing an embryo – are avoidable. It is unclear at this writing whether any concerted effort has been made to validate the safety and efficacy of PGD by objective research from the perspective of whether embryo extractions are safe.

- ❖ *Advances in the field of IVF – Mitochondrial donation:* Assisted reproductive technologies have recently been expanding into a new market of embryo donation, making it possible to use donor mitochondria in an IVF treatment in order to prevent women who carry a disease caused by mitochondrial mutation from transmitting the disease to their children. Mitochondrial⁷⁶ DNA (mtDNA) mutations are associated with a broad range of debilitating and fatal diseases and disorders such as muscular dystrophy, Leber hereditary optic neuropathy (LHON) and Leigh syndrome.⁷⁷ Mitochondrial DNA diseases are considered to be among the most common genetic disorders and at present there is no cure for such diseases.⁷⁸ However, there may be a way to prevent them by genetically altering the eggs or

⁷³ Recent studies suggest that it is more advantageous to perform biopsy on an embryo at the blastocyst stage (day 5) than sampling done in day 3. John A Robertson, 'Extending Preimplantation Genetic Diagnosis: The Ethical Debate Ethical Issues in New Uses of Preimplantation Genetic Diagnosis' (2003) 18 Human Reproduction 465. Elena E Zakharova, Victoria V Zaletova and Alexander S Krivokharchenko, 'Biopsy of Human Morula-Stage Embryos: Outcome of 215 IVF/ICSI Cycles with PGS' (2014) 9 PLoS ONE.

⁷⁴ Claudia Carr, *Beginning Medical Law* (Routledge 2015) 102–103. John A Robertson, 'Extending Preimplantation Genetic Diagnosis: The Ethical Debate Ethical Issues in New Uses of Preimplantation Genetic Diagnosis' (2003) 18 Human Reproduction 465.

⁷⁵ Andrea Borini, Nicoletta Tarozzi and Cristina Lagalla, 'Preimplantation Genetic Diagnosis: Why Are Obstetric and Neonatal Risks Increased? The Need for More Data' (2016) 106 Fertility and Sterility 1328. Richard T Scott and others, 'Cleavage-Stage Biopsy Significantly Impairs Human Embryonic Implantation Potential While Blastocyst Biopsy Does Not: A Randomized and Paired Clinical Trial' (2013) 100 Fertility and Sterility 624. Bjorn Bay and others, 'Preimplantation Genetic Diagnosis: A National Multicenter Obstetric and Neonatal Follow-up Study' [2016] Fertility and Sterility.

⁷⁶ Mitochondria are tiny organelles in the cytoplasm of all nucleated cells.

⁷⁷ Louise A Hyslop and others, 'Towards Clinical Application of Pronuclear Transfer to Prevent Mitochondrial DNA Disease' (2016) 534 Nature 383. Eric A Schon, Salvatore DiMauro and Michio Hirano, 'Human Mitochondrial DNA: Roles of Inherited and Somatic Mutations' (2012) 13 Nature Reviews. Genetics 878.

⁷⁸ See Andrew M Schaefer and others, 'Prevalence of Mitochondrial DNA Disease in Adults' (2008) 63 Annals of Neurology 35, 35. Hannah R Elliott and others, 'Pathogenic Mitochondrial DNA Mutations Are Common in the General Population' (2008) 83 American Journal of Human Genetics 254, 254.

embryos through a procedure known as mitochondrial donation. Mitochondrial DNA is inherited solely through the maternal line, and the available technique can be used to prevent women from passing on devastating and often fatal genetic diseases to their children by making IVF embryos that have the normal set of chromosomes from the parents, but healthy mitochondria from a donor. Mitochondrial replacements raise controversial issues because it will result in an embryo that has nuclear DNA from both parents and mitochondrial DNA from a donor, otherwise known as “three-parent babies”. In February 2015, the British Parliament amended the relevant legislation, making UK the first country in the world to allow mitochondrial donation during IVF in situations where a child is at risks of inheriting a serious mitochondrial disorder.⁷⁹ Even though the UK is the first country in the world authorizing the procedure, there are indications that the practice might be carried out in many other countries with no regulation relating to mitochondrial donation, such as Mexico, where in April 2016, the first child was born out of this procedure.⁸⁰

3.2.2 Analysis

Much of the initial legal scrutiny of ART has focused on challenges made possible not only by the technology itself but the way in which the technology has been used or created problems for legal rules. For example, the use of ART as a means of sex selection of the child has been criticized as a form of discrimination with broad stigmatic effects and is currently prohibited on non-medical grounds by Article 14 of the Convention on Human Rights and Biomedicine.⁸¹ The use of anonymous donors and surrogates has generated considerable concern about the rights of children to information, not only regarding identity and to know one’s parents, but in part in relation to who is legally registered by law as the child’s parents.⁸² In rare cases, the use of ART for particular purposes, such as to create “savior siblings” has raised questions about whether the physical integrity of the child is put at stake by such uses of ART, as further elaborated in Chapter 7.⁸³ These debates, however, are often difficult to disentangle from conflicting legal norms – such as the freedom to terminate a pregnancy for sex selection purposes, the right to anonymity for those who give up their children for adoption, or the general right of parents to procreate and consent to health-related interventions on their children.

Nevertheless, many of the rights of the child that have been identified by these former controversies take on greater significance because of the scientific uncertainties of ART itself:

- ❖ *The right to information relative to identity and familial connections:* As with questions over the rights of adopted children to know their biological parents, considerable discourse has been generated regarding the right of children born via ART to know their origins as part of the *right to know one’s parents* and the *right to private life*. Scientific advances, such as mitochondrial donations with IVF, amplify the complexity of these questions when multiple donors are

⁷⁹ See the amended Human Fertilization and Embryology Act 1990 and the Human Fertilization and Embryology Act 2008. See also Samvel Varvaštian, ‘UK’s Legalisation of Mitochondrial Donation in IVF Treatment: A Challenge to the International Community or a Promotion of Life-Saving Medical Innovation to Be Followed by Others?’ (2015) 22 European Journal of Health Law 405.

⁸⁰ J Zhang and others, ‘First Live Birth Using Human Oocytes Reconstituted by Spindle Nuclear Transfer for Mitochondrial DNA Mutation Causing Leigh Syndrome’ (2016) 106 Fertility and Sterility e375.

⁸¹ See also Council of Europe Parliamentary Assembly, Resolution 1829 (2011) Prenatal sex selection, para 7. Council of Europe Parliamentary Assembly, Recommendation 1979 (2011) Prenatal sex selection. Marcy Darnovsky, ‘Countries with Laws or Policies on Sex Selection’ [2009] Memorandum, April, Center for Genetics and Society, Berkeley, CA.

⁸² For a survey of the issues, see Jane Stoll, *Swedish Donor Offspring and Their Legal Right to Information* (Uppsala University, 2008). See Jane Stoll, ‘Donor Offspring and the Right Not to Know: An Argument against Permitting Full Genetic Donor Siblings?’ in Anna Singer and Marie Linton (eds), *Förnuft, känsla och rättens verklighet* (Iustus förlag 2014). See also Michelle Giroux, Juliet Ruth Guichon and Ian Mitchell, *The Right to Know One’s Origins: Assisted Human Reproduction and the Best Interests of Children* (2012) 263–265.

⁸³ Malcolm K Smith, *Saviour Siblings and the Regulation of Assisted Reproductive Technology: Harm, Ethics and Law* (Routledge 2016) 116–124.

involved in creating a single child. Some of these problems are created not by the technology itself but by national laws – for example, those that shield donors from registration as parents or only recognize parents based on marital or adoptive status rather than biology. However, when a child has an interest in receiving information relative to its health, the medico-legal justifications for nondisclosure are much more problematic if the identity of the donors could be protected even when disclosure of the health-related information could be compelled.⁸⁴

A child's claim of right to information about its parents could thus be strengthened if a link to the child's health is established and recognized as encompassed by the *right to the highest attainable standard of health (right to health)*.⁸⁵ That right is not only a core human right but generally includes the right to access to health-related information.⁸⁶ In the case of ART, any right to information may be compromised in several ways. It may be impaired by the concealment of a donor or surrogate. It may also be impaired by what the parents as ART consumers or patients were told regarding the process or what information they declined to consider. In the first instance, if the surrogate mother or egg donor transmits a gene implicated in a certain disease, such as cancer, a lack of knowledge of the information could affect the ability of the child to test and protect against such risk.⁸⁷ In the latter, failure of the ART provider to disclose risks from a particular procedure or the failure of parents to take an interest in the information may impair the child's access to essential health-related information about the risks that accompanied the child's creation. Censoring or withholding health-related information might, therefore, be viewed as an interference with the right to health, especially in situations when the information is needed in order for the child of the donor recipient to obtain appropriate healthcare.⁸⁸

- ❖ *The right to the highest attainable health of the prospective child:* To date, very little legal discourse has focused on the rights of the child to ensure that ART does not in itself involve health risks for the created child. For example, in the case of the use of GnRH analogues (mentioned in 3.2.1), current recommendations focus on the right of the parents to informed consent about damage to the embryo or fetus. The challenges that ART poses to the right to the highest attainable standard of health are complex. On the one hand, ART providers may make no general assurances about the health of offspring – even though techniques such as PGD are designed to determine if the child is likely to have a severe illness or disability. At the same time, however, to the extent states have positive obligations to promote the health of children and protect them from harm, it is unclear whether the investigation of the risks by particular ART techniques should be left solely to practitioners, particularly as much ART takes place in state-run hospitals or minimally regulated private facilities. Both medical liability rules and the right of informed consent varies from jurisdiction to jurisdiction, such that it remains unclear to what extent these rights of the consumer-parents will extend to the child and ensure any remedies from harmful practices.
- ❖ *The right to protection from discrimination:* With the establishment of the Convention on Human Rights and Biomedicine, it can no longer be argued that ART practices are exempt from all discrimination prohibitions in selecting which children might be born, given that the

⁸⁴ See, for example, Rebecca Dimond, 'Techniques of Donation: "Three Parents", Anonymity and Disclosure' (2015) 3 Journal of Medical Law and Ethics 165.

⁸⁵ More generally on the right to health see Kavot Zillén, *Hälsa- och sjukvårdspersonalens religions- och samvetsfrihet: En rättsvetenskaplig studie om samvetsgrundad vägran och kravet på god vård* (Uppsala University 2016) ch 3.

⁸⁶ Giroux, Guichon and Mitchell (n 82) 252, 254.

⁸⁷ Petra De Sutter, report on *Children's rights related to surrogacy*, Committee on Social Affairs, Health and Sustainable Development, the Parliamentary Assembly of the Council of Europe, Provisional version 21 September 2016, 8–9.

⁸⁸ John Tobin, *The Right to Health in International Law* (Oxford University Press 2012) 188. Michelle Giroux, Juliet Ruth Guichon and Ian Mitchell, *The Right to Know One's Origins: Assisted Human Reproduction and the Best Interests of Children* (2012) 225.

Convention now prohibits the use of medically assisted procreation techniques for non-medical reasons as a form of discrimination.⁸⁹ With ongoing concern that the practice is occurring in Europe,⁹⁰ human rights agencies have made clear that the concern for these practices is that they promote neglect of girls and different treatment of children based on gender,⁹¹ and stigmatizing girls and women as having lower status, contrary to *the principle of human dignity and equality*.⁹² Nevertheless, the symmetry between this form of discrimination in the context of children born of ART may not be easy to establish for other forms of status based selection of which children should be born, depending on how general rules about eugenic practices are formulated.⁹³ The diagnostic technology might be considered as a discriminatory practice that stigmatizes children with certain disorders or disabilities.⁹⁴ However, unlike when ART is used effectively to produce more male children by supporting parent's individual gender preferences, the goal of producing healthy children and sparing children disability may be seen as substantively different, if safe and effective in doing so.

More problematic, however, is how children born with anomalies or other impairments might be perceived as wrongful births after ART, whether or not particular jurisdictions permit such causes of actions. Regardless of whether ART causes impairments or anomalies, the expectations created by these practices leaves unclear how children born with those impairments or anomalies will be treated, especially within their families. Particularly if ART techniques cause physical impairments to the future child, the risk of subjecting children to disabilities and the risk of discrimination and stigmatization warrants further inquiry.⁹⁵

3.3 Corrective procedure in utero

3.3.1 Scientific background

Since the late 1970s, when real-time ultrasound was first introduced, different types of fetal therapy techniques used for diagnosing and treating fetal anomalies have been developed.⁹⁶ Various fetal diseases and disorders, including cardiac arrhythmias, structural abnormalities, fetal metabolic diseases and abnormalities of placental vessels and membranes, in theory, can be managed by medical and surgical fetal interventions. The difficulty with such interventions is that surgery on the fetus entails significant risks to the future child as well as the mother, whereas other interventions may affect the child when at a highly vulnerable stage of development. As a result, less invasive procedures are currently developed, though they too remain experimental. Gene replacement therapy for cystic fibrosis, for example, currently is not in use because of mutagenesis in animal studies.⁹⁷ When a future child has been diagnosed with a serious physical

⁸⁹ See the Parliamentary Assembly of the Council of Europe resolution 1829, *Prenatal sex selection* (n 81).

⁹⁰ In recent years it has been reported that a number of Council of Europe member states, such as Albania, Armenia, Azerbaijan and Georgia has problems with imbalanced sex ratios, indicating the usage of sex-selective practices, though unclear whether they result from ART. *ibid*.

⁹¹ WHO, Department of Reproductive Health and Research, *Preventing gender-biased sex selection: an interagency statement OHCHR, UNFPA, UNICEF, UN Women and WHO* (WHO, 2011), 5.

⁹² Steering Committee on bioethics report, *The protection of human embryo in vitro* (CDBI-CO-GT3, 2003), 13; WHO (n 76) 3.

⁹³ Article 3.2 in The Charter of Fundamental Rights of the European Union contains a prohibition of "eugenic practices", which has been discussed in relation to PGD.

⁹⁴ Jaime S King, 'Predicting Probability: Regulating the Future of Preimplantation Genetic Screening?' (2008) 8 *Yale journal of health policy, law, and ethics* 283, 358.

⁹⁵ *ibid* 340. Kristin Savell and others, *Perfecting Pregnancy: Law, Disability, and the Future of Reproduction* (Cambridge University Press 2012). T Petersen, 'Just Diagnosis? Preimplantation Genetic Diagnosis and Injustices to Disabled People' (2005) 31 *Journal of Medical Ethics* 231.

⁹⁶ Mark D Kilby, Anthony Johnson and Dick Oepkes, *Fetal Therapy: Scientific Basis and Critical Appraisal of Clinical Benefits* (Cambridge University Press 2013) 1.

⁹⁷ Kevin Nishida and others, 'Cystic Fibrosis: A Look into the Future of Prenatal Screening and Therapy' (2015) 105 *Birth Defects Research. Part C, Embryo Today: Reviews* 73.

disability or congenital anomaly at the fetal stage, however, clinicians have increasingly used corrective procedures *in utero* on the grounds that the risks of the child of being born with the anomaly justify the intervention, despite the scientific uncertainty.

In utero surgery

In utero surgery has been practiced since the late 1980s and is today used to treat some congenital diseases such as *monochorionic twin gestation complications*,⁹⁸ *congenital cystic adenomatoid malformation of the lung*,⁹⁹ and *congenital diaphragmatic hernia*.¹⁰⁰ Further, even though perception and processing of fetal pain are not well understood, fetal surgery may demand the usage of anesthetic techniques to facilitate these invasive procedures.¹⁰¹ Providing anesthesia and fetal pain relief for fetal surgery is challenging for many reasons, mainly because it requires integration of both obstetric and pediatric anesthesia practice.¹⁰² Even among proponents of fetal surgery, the risks of the intervention itself, along with the risks of anesthesia, have led to calls within the surgical community that the procedures only be done by expert centers and in limited cases where no other options are available.

An example of fetal surgery has also been practiced to treat the most severe and common form of *spina bifida* or *myelomeningocele*, which occurs *in utero* during the early period of embryonic development, where the spine has failed to fuse into a unified structure and is unprotected by skeletal muscle.¹⁰³ Because the spine is not fully formed, it is, thus, exposed to fluid. Thus, the spine and its nerves can become damaged *in utero* or other complications with growth manifest as the fetus develops, such as paralysis, ambulatory disabilities, neurological side effects and high rates of childhood mortality. Until recently, standard treatment options have been limited to (1) surgery immediately after birth, (2) caesarean delivery to perform surgery before natural birth, or (3) abortion. In the US and Europe, the Management of Myelomeningocele Study, dubbed “MOMS”, attempted to determine if fetal surgery could repair the spine and prevent critical nerve damage and paralysis, even though that surgery is considered technically challenging and inherently high-risk to both mother and the fetus.¹⁰⁴ Some of the fetuses died or suffered injury in the study and mothers have suffered several complications. The clinicians leading the MOMS study and its successors have reported, however, that the majority of young children show significantly less short-term ambulatory problems and normal childhood function because of fetal intervention. Though its proponents concede that the surgery should only be performed by experts and needs refining, they continue to recommend it as “novel” surgery.¹⁰⁵

⁹⁸ The condition is also known as “Twin-to-twin transfusion syndrome” (TTTS) in which identical twins sharing an umbilical cord do not have equal access to nutrients from the mother's blood.

⁹⁹ This condition is a rare abnormality of lung development that requires invasive surgery.

¹⁰⁰ This condition is a defect in the development of the fetal diaphragm that can be treated using video fetoscopic technology surgery, Diana Farmer, ‘Fetal Surgery’ (2003) 326 *BMJ*: British Medical Journal 461.

¹⁰¹ Alan Cameron, *Fetal Medicine for the MRCOG and beyond* (RCOG Press 2011) 108. J Deprest and others, ‘The Fetal Patient – Ethical Aspects of Fetal Therapy’ (2011) 3 *Facts, Views & Vision in ObGyn* 221.

¹⁰² Elaina E Lin and Kha M Tran, ‘Anesthesia for Fetal Surgery’ (2013) 22 *Seminars in Pediatric Surgery* 50.

¹⁰³ T Kohl, ‘Percutaneous Minimally Invasive Fetoscopic Surgery for Spina Bifida Aperta. Part I: Surgical Technique and Perioperative Outcome’ (2014) 44 *Ultrasound in Obstetrics & Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology* 515. Spina bifida is a fetal neural tube defect (NTD), which may be diagnosed in utero. The defect is compatible with significant disability and morbidity.

¹⁰⁴ For the trials see Kelly A Bennett and others, ‘Reducing Perinatal Complications and Preterm Delivery for Patients Undergoing in Utero Closure of Fetal Myelomeningocele: Further Modifications to the Multidisciplinary Surgical Technique: Clinical Article’ (2014) 14 *Journal of Neurosurgery: Pediatrics* 108. Kelly A Bennett and others, ‘Reducing Perinatal Complications and Preterm Delivery for Patients Undergoing in Utero Closure of Fetal Myelomeningocele: Further Modifications to the Multidisciplinary Surgical Technique: Clinical Article’ (2014) 14 *Journal of Neurosurgery: Pediatrics* 108, 108.

¹⁰⁵ E Araujo Júnior and others, ‘Procedure-Related Complications of Open vs Endoscopic Fetal Surgery for Treatment of Spina Bifida in an Era of Intrauterine Myelomeningocele Repair: Systematic Review and Meta-Analysis’ (2016) 48 *Ultrasound Obstet Gynecol* 151.

As with the case of fetal surgery, the medical literature makes clear that non-surgical intervention on the fetus – such as the use of medication *in utero* – is taking place in clinical practice, not necessarily in the context of carefully supervised research. For the rare condition of *fetal goiter*, for example, detection of the condition led to the sporadic use of injections of medication, such as intra-amniotic levothyroxine, into the amniotic fluid to reach the affected fetus.¹⁰⁶ Though this appears to have become common practice, the number of such cases, however, is so small that treatment recommendations lack data for predictable outcomes, compared with anecdotal alternatives, such as preterm delivery and treatment to prevent complications from the condition.¹⁰⁷ In cases of *fetal cardiac arrhythmias*, intravenous injection of medication into the fetal cord or intramuscular injection into the fetal thigh or buttock has been used anecdotally to improve fetal survival, though here too carefully developed protocols do not exist.¹⁰⁸ For *fetal anemia*, in utero blood transfusions to replace fetal red blood cells with some success, though random use has resulted in severe complications and fetal death.¹⁰⁹ Because the use of medication on children after birth itself is considered to entail significant risks without careful testing of uses of these products, the use of these procedures in clinical practice raises significant questions about how these treatments may progress to standard care.

Even without regard to the inherent risk of using medication during the earliest stages of human development, however, the use of these therapies raises questions about whether the risk to the patient is actually in the interest of the future child. Where a fetus is at risk of *congenital adrenal hyperplasia* (CAH), parents have been offered administration of dexamethasone (DEX) *in utero*, in order to prevent genetically female children with CAH from virilizing, which is perceived as an intersex condition in which the child's clitoris appears more masculine – in many cases where the child appears typically male and may even identify as male. While some forms of CAH are life-threatening, fetal-DEX is only designed to respond to the virilizing condition in the affected children – primarily to avoid the surgeries and other “gender-normalizing” interventions now criticized as human rights violations, as discussed in Chapter 5. The full extent of the risks, however, are unknown, as physical sex differentiation in children begins very early in pregnancy, such that the hormone would apply at a time when the child's brain is only beginning to form. Long-term follow-up has shown that the children subjected to the hormone have impaired cognitive development.¹¹⁰ Moreover, while many of the genetically female children were born without virilization, the genetically male children have exhibited signs of gender atypicality, confirming suspicions that hormonal impacts *in utero* affected gender development in the brain.¹¹¹ Despite these outcomes, only one leading hospital, Sweden's Karolinska Institute, has formally called for the restrictive use of the drug as an experimental treatment without evidence of benefit to each individual child.¹¹²

¹⁰⁶ Min-Jung Kim and others, 'Intra-Amniotic Thyroxine to Treat Fetal Goiter' (2016) 59 *Obstetrics & Gynecology Science* 66.

¹⁰⁷ Ümit Göktolga and others, 'Intrauterine Fetal Goiter: Diagnosis and Management' (2008) 47 *Taiwanese Journal of Obstetrics and Gynecology* 87.

¹⁰⁸ Bettina F Cuneo, 'Fetal Atrial Flutter and Hydrops Successfully Treated with Transplacental and Direct Fetal Therapy' (2016) 6 *Prenatal Cardiology* 16. Janette F Strasburger and Ronald T Wakai, 'Fetal Cardiac Arrhythmia Detection and in Utero Therapy' (2010) 7 *Nature Reviews. Cardiology* 277.

¹⁰⁹ Lucie Guilbaud and others, 'In Utero Treatment of Severe Fetal Anemia Resulting from Fetomaternal Red Blood Cell Incompatibility: A Comparison of Simple Transfusion and Exchange Transfusion' (2016) 201 *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 85. C Garabedian and others, 'Neonatal Outcome after Fetal Anemia Managed by Intrauterine Transfusion' (2015) 174 *European Journal of Pediatrics* 1535.

¹¹⁰ Heino FL Meyer-Bahlburg and others, 'Cognitive Outcome of Offspring from Dexamethasone-Treated Pregnancies at Risk for Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency' (2012) 167 *European Journal of Endocrinology* 103. Tatja Hirvikoski and others, 'Prenatal Dexamethasone Treatment of Children at Risk for Congenital Adrenal Hyperplasia: The Swedish Experience and Standpoint' (2012) 97 *The Journal of Clinical Endocrinology and Metabolism* 1881.

¹¹¹ Hirvikoski and others (n 110).

¹¹² *ibid* 1882.

3.3.2 Analysis

In theory, the benefit of different forms of fetal interventions or corrective procedures in utero lies first and foremost in the ability to diagnose and treat congenital anomalies at an early stage of human development, preventing such harms as irreversible organ damage or fetal death. As the technology of ultrasound equipment has become more sophisticated the possibilities of planning and performing different interventions for early fetal diagnosis and therapy has increased.¹¹³ The right of access to care is often interpreted to include access to preventive medicine for young children before they are born, strengthening preventive health care before pregnancy and for mothers and babies in pre- and post-natal, pediatric care.¹¹⁴ At the same time, the lack of ample, long-term evidence of safety and efficacy of these corrective procedures in utero gives rise to important human rights concerns with regards to the level of risk taken to the child's physical health. Given the well-known problems associated with the effects of treatments *in utero* from treatments ranging from *thalidomide* for treating certain cancers to *progesterin* to help prevent premature birth, the risks of intervention during the earliest stages of human development should be apparent.

Though many of these procedures may be well-intentioned, questions remain as to how these procedures strike a balance between the right to *the highest attainable standard of health*, on the one hand, and *the right to physical integrity and freedom from experimentation* on the other. For fetal surgery, the justification typically offered is that the risks of the interventions are often balanced against the severity of the disability and the potential for termination of the pregnancy. While there is little question that the effort is designed to bring the child to birth spared from disability, it is also clear that the procedures risk other injuries to that same child. Questions, therefore, remain whether the risk to the child's health is warranted in the absence of further research, even though research on the fetus itself may be difficult until animal studies or computer simulations are done. Regarding fetal medication, the administration of *levothyroxine* directly to the fetus in cases of the treatment of fetal goiter may seem to represent a good example of preventive care, even though it seems that the testing has occurred through clinical experience and not through carefully supervised clinical trials. To prevent possible harm to the future child and violations of children's human dignity, it remains unclear whether these procedures should be permitted in practice without careful testing or oversight.¹¹⁵

More problematically, however, the use of prenatal interventions in the case of *fetal-DEX* to avoid genital anomalies raises more serious questions about whether these interventions are being done to spare the child from harm or to serve other interests. Even apart from concerns about the motive of surgery (for the benefit of the parent), the lack of long-term studies about the effectiveness and safety of these procedures raises questions about why their use is permitted as a matter of clinical practice as well as a matter of law. In one of the few studies with long-term follow-up, a number of neuropsychological consequences were found, indicating the possibility of more harmful effects. Though the treatment was intended to prevent genital surgery in affected female infants to make them more "normal" for their sex, the genital surgery itself, along with other normalization procedures, is now sharply criticized on human rights and scientific grounds, as explained in Chapter 5.¹¹⁶

In sum, the complexity of these interventions raises a series of questions that as yet appear unaddressed in clinical practice: (1) when must these procedures be carefully tested before their

¹¹³ Radu Vladareanu and Vlad Zamfirescu, 'Invasive Fetal Surgery – A Medical and Ethical Challenge of Our Time' 56.

¹¹⁴ See Resolution 1829, Prenatal sex selection, § 9.8 (n 81).

¹¹⁵ Paolo Sala and others, 'Fetal Surgery: An Overview' (2014) 69 *Obstetrical & Gynecological Survey* 218.

¹¹⁶ *ibid.*

use with patients and (2) how clear should the benefit be before the interventions take place, given that any intervention at the earliest stages of development may generate unpredictable adverse outcomes, regardless of the intervention at stake. Given the potential disability or disfavor for the child's conditions, questions should also be raised as to whether the unusual risks that are taken at these stages would otherwise be taken for other children as a matter of good clinical practice, or because the potential parental rejection of the child with the condition is used to justify those risks.

3.4 Summary of the rights at stake

The increasing technological advances in the field of ART and prenatal therapies are designed to facilitate the creation of healthy children. In the case of prenatal therapies, many interventions are specifically designed to treat or prevent conditions with the intent to improve the health of the child. Nevertheless, these interventions raise a series of challenges for rights in relation to biomedicine because they take place before the child is born. The timing of these interventions inherently causes interventions at the earliest stage of the development, where much is known about the fragility of the developmental stage of the future child, but little is often known about what specific effects they might have on the child. As a result, the physical health of the child is at stake in interventions that often are designed to promote the interests of the parents, or where it is unclear whether risks are taken in interventions for various reasons that may not be considered acceptable after the child is born.

In the light of the above-described scientific challenges regarding these technologies and procedures, some fundamental rights of the child seems to be of particular importance in this field, which is demonstrated in the chart below:

Scientific challenge/procedure	Rights at stake
ART	<ul style="list-style-type: none"> ● Right to identity ● Right to autonomy and private life ● Right to the highest attainable standard of health ● Right to equality and non-discrimination
Fetal surgery	<ul style="list-style-type: none"> ● Right to physical integrity ● Right to highest attainable standard of health ● Protection for human dignity
In utero administration of medication	<ul style="list-style-type: none"> ● Right to physical integrity ● Right to highest attainable standard of health ● Protection for human dignity



4 Genetics: analysis, therapy and technology

4.1 Introduction

Perhaps more than any other biomedical field, genetics has the greatest potential to affect children beyond clinical practice. Indeed, from a clinical perspective, pediatric genetics is one of the very few specialties that had its origins outside of the practice of medicine.¹¹⁷ Many advances in the field of genetics continue to originate outside the clinical context. Multinational projects to map the human genome, such as Human Genome Project¹¹⁸ and HapMap¹¹⁹ have generated unprecedented knowledge about the human genome, from which many clinical applications are now being developed.¹²⁰ Today, genetic analysis can be done for a wide variety health-related and non-health related purposes, both within and outside the traditional clinical setting. In fact, it is now possible to target single genes and ascertain their meaning regarding human health, behavior, and phenotypes, as well as in some cases take early steps for tackling medical conditions. As a result, it should not be surprising that the field of genetics has been adapted into pediatric medicine as a means to better understand diseases, disorders, and developmental differences, so that adverse medical conditions may be identified and treated as soon possible.

Genetic testing could, in principle, also be used in pediatric care, though the prevailing view, except for matters of medical necessity, has been that predictive genetic testing should be deferred until the minor can consent. Genetic databases are being developed for a broad spectrum of conditions, both physiological and psychological. Especially for rare diseases, these resources are considered essential to understanding and improvement of care for children. The future of genetics in clinical practice, on the other hand, is difficult to foresee.¹²¹ Of considerable concern, genetic analysis is ongoing for conditions discussed elsewhere in this report, but without clear indicators of whether it will be used to further questionable interventions or to develop new and unpredictable ones on vulnerable children.¹²²

This chapter focuses on several applications of genetics where scientific advances or uncertainties exist to illustrate where the rights of children may be at stake and where genetic advances may be heading in the future. The chapter begins with an examination of health-related genetic testing that may be offered to consumers outside of a clinical setting, here described as *health-related direct-to-consumer genetic testing*. Next, the chapter continues with an analysis of non-invasive genetic testing or *NIPT*, which has been developed as an alternative to other invasive forms of genetic testing in clinical settings. This is followed by a brief summary of *whole genome sequencing* (WGS) and *whole exome sequencing*, and the uncertainties of how it will be applied in clinical practice,

¹¹⁷ David L Rimoin and Kurt Hirschhorn, 'A History of Medical Genetics in Pediatrics' (2004) 56 *Pediatric Research* 150.

¹¹⁸ W Gregory Feero, Alan E Guttmacher and Francis S Collins, 'The Genome Gets Personal--Almost.' (2008) 299 *JAMA* 1351.

¹¹⁹ Richard A Gibbs and others, 'The International HapMap Project' (2003) 426 *Nature* 789.

¹²⁰ Eric S Lander, 'Initial Impact of the Sequencing of the Human Genome' (2011) 470 *Nature* 187.

¹²¹ Christopher H Wade, Beth A Tarini and Benjamin S Wilfond, 'Growing Up in the Genomic Era: Implications of Whole-Genome Sequencing for Children, Families, and Pediatric Practice' (2013) 14 *Annual review of genomics and human genetics* 535.

¹²² For differences in sex development and intersex conditions, see Valerie A Arboleda, David E Sandberg and Eric Vilain, 'DSDs: Genetics, Underlying Pathologies and Psychosexual Differentiation' (2014) 10 *Nature Reviews Endocrinology* 603. For schizophrenia, Systematic meta-analyses and field synopsis of genetic association studies in schizophrenia see Jennifer L Stone and others, 'Rare Chromosomal Deletions and Duplications Increase Risk of Schizophrenia' (2008) 455 *Nature* 237. These conditions are discussed in Chapters 5.2 and 6.3, respectively.

exemplified by what is known as the BabySeq Project, which will apply the technology to diagnosis and treatment of newborns. Finally, the chapter surveys technology that will transcend mere analysis of the human genome and the use of gene-based innovations in reproductive technologies, going much further than before with gene modification for therapeutic and enhancement purposes.¹²³ The potential for creating a human synthetic genome has also recently been proposed.¹²⁴ The overarching aim of this chapter is to illustrate the many ways that these applications may affect the rights of children, both in and outside of general clinical practices.

4.2 Health-related direct-to-consumer genetic testing

4.2.1 Scientific background

Genetic testing has historically been carried out utilizing a cellular sample of the person being tested to extract genetic data and analyze it. The testing often takes place in a clinical setting (through a healthcare provider or as a drop-in laboratory service) but is now increasingly offered as part of direct-to-consumer genetic testing services. This latter form of testing has become an increasingly popular method of supply of genetic analysis to consumers without either direct or mandatory involvement of a healthcare provider, who can act as an intermediary in utilizing the test and can help the consumer understand the results.¹²⁵ There are various forms of direct-to-consumer genetic testing, such as tests bought over the counter in a pharmacy or on the Internet.¹²⁶

In the scientific community, the following elements have been identified as crucial for genetic analysis: analytical and clinical validity, clinical utility, and assessment of ethical, legal and societal issues (ELSI). These requirements have also been endorsed for direct-to-consumer genetic testing.¹²⁷ To ensure accurate functioning of a test and its value in healthcare, the first three of these are of critical importance. Analytical validity focuses on the laboratory component, indicating the correlation between the test results and the targeted sequence.¹²⁸ Clinical validity refers to the test's ability to detect a disorder for which the test is offered (and for predictive tests, to predict the likelihood of the disorder).¹²⁹ For the test to be clinically valid, there should be a proven link between the genetic markers and the condition for which a consumer is tested.¹³⁰ The third criterion is utility, which can be perceived in two ways – either broadly or narrowly. A narrow understanding of utility focuses on the clinical application of the testing,

¹²³ Moira A McMahon, Meghdad Rahdar and Matthew Porteus, 'Gene Editing: Not Just for Translation Anymore' (2011) 201 *Nature* 2.

¹²⁴ Amber Dance, 'Synthetic Human Genome Set to Spur Applications' (2016) 34 *Nature Biotechnology* 796.

¹²⁵ Santa Slokenberga, 'Direct-to-Consumer Genetic Testing: Changes in the EU Regulatory Landscape' (2015) 22 *European Journal of Health Law* 463.

¹²⁶ There might not be considerable differences between these two types, as some tests that are sold over the Internet are also sold through a pharmacy chain (for example, in Sweden certain kinds of direct-to-consumer genetic tests can be purchased in Apoteket pharmacy chain). Compare Apoteket, <https://www.apoteket.se/produkt/apoteket-anlag-for-overvikt-1-st-254589/www.dynamiccode.se> and 23andMe, <https://www.23andme.com/en-eu/>, accessed 22 August 2016.

¹²⁷ The ACCE framework was developed by the US institutions – the Centers for Disease Control and Prevention, National Office of Public Health and the Foundation of Blood Research. These criteria have been endorsed by several institutions in various states. It has been endorsed, for example, by the collaborative initiative of the Public and Professional Policy Committee of the European Society of Human Genetics, EuroGentest, and the Institute for Prospective Technological Studies, which one or another way, they are related to the EU and its policy (making) regarding genetic testing. Frauke Becker and others, 'Genetic Testing and Common Disorders in a Public Health Framework: How to Assess Relevance and Possibilities' (2011) 19 *European Journal of Human Genetics* S6, s15.

¹²⁸ Wylie Burke, 'Genetic Tests: Clinical Validity and Clinical Utility' (2014) 81 *9.15.1*.

¹²⁹ Becker and others (n 127), with a further reference to Public Health Genomics at Centers for Disease Control and Prevention, http://www.cdc.gov/genomics/gtesting/ACCE/acce_proj.htm#T1, accessed 10 November 2016.

¹³⁰ Kathy Hudson and others, 'ASHG Statement on Direct-to-Consumer Genetic Testing in the United States' (2007) 81 *American Journal of Human Genetics* 635.

namely clinical utility.¹³¹ A broad understanding of utility would consider not only the clinical utility of testing but also whether the outcome of a test can be of any assistance to the individual concerned in their decisions.¹³²

For the purposes of direct-to-consumer genetic testing, a wide range of technologies has been used. This can be broadly classified as follows: (1) genotyping or targeted analysis of a small number of specific genetic variants, (2) the use of a “single nucleotide polymorphism” (SNP),¹³³ or (3) sequencing of the DNA, either to determine the sequence of bases or the whole genome.¹³⁴ Panel-based analysis is predominantly offered in direct-to-consumer genetic testing.¹³⁵ However, many companies purport to offer other techniques as services, such as whole exome sequencing¹³⁶ and whole genome sequencing.¹³⁷ Each of these techniques entails different degrees of examination of the person’s genome and, accordingly, different degrees of intervention with the person’s private sphere. While the SNP analysis allows targeting a particular part of the human genome and is aimed at variations of a single gene within the genome, whole genome sequencing as its name suggests reaches an individual’s whole genome, in such a way interfering with the person’s private sphere at the highest degree.

4.2.2 Analysis

Direct-to-consumer genetic testing marks a significant change in the provision of healthcare services. As the testing is generally done without the involvement of a healthcare provider, the commercial providers of the test typically claim that they are not providing a health service and, therefore, are not subjected to the relevant regulatory requirements.¹³⁸ However, because they offer a test that can be used for health-related purposes through the delivery of predictive genetic information, by many definitions these tests can be regarded a healthcare service and could be addressed accordingly.¹³⁹

A key concern of direct-to-consumer genetic testing on children rests with clinical validity and utility of these tests, as well as with the method of supply. The questions that relate to the quality of genetic testing within the Council of Europe legal order are addressed explicitly in the Additional Protocol on Genetic Testing, whereas in the EU legal order they are addressed through Directive 98/79/EC and through the Proposal for a Regulation on *In vitro* diagnostic medical devices.¹⁴⁰ While the Additional Protocol on Genetic Testing in detail addresses situations in which a minor can be subjected to testing, it is unclear how effective these requirements are in light of the method of supply of these tests. Direct-to-consumer genetic

¹³¹ Scott D Grosse and Muin J Khoury, ‘What Is the Clinical Utility of Genetic Testing?’ (2006) 8 *Genetics in Medicine* 448, 448. Becker and others (n 127). with a further reference to Centers for Disease Control and Prevention (n 129).

¹³² Grosse and Khoury (n 131) 448. Becker and others (n 127)., with a further reference to Centers for Disease Control and Prevention (n 129).

¹³³ A single-nucleotide polymorphism or SNP is a variation in a single nucleotide that occurs at a specific position in the genome, often a strong indicator of a particular condition, such as a disease that has been identified by comparing persons with the condition to those without it, identified by comparison of regions of the genome.

¹³⁴ Sancy A Leachman and others, ‘Direct-to-Consumer Genetic Testing: Personalized Medicine in Evolution’ *Journal of Clinical Oncology*.

¹³⁵ For example, 23andMe, <https://www.23andme.com/more/genotyping/>, accessed 22 August 2016.

¹³⁶ Exome 80x Pilot project offered by 23andMe in 2011. 23andMe, <http://blog.23andme.com/news/announcements/exomes-the-first-of-many/>, accessed 22 August 2016.

¹³⁷ List of personal genomics companies. International Society of Genetic Genealogy, http://www.isogg.org/wiki/List_of_personal_genomics_companies, accessed 22 August 2016.

¹³⁸ Cynthia Marietta and Amy L McGuire, ‘Direct-to-Consumer Genetic Testing: Is It The Practice of Medicine?’ (2009) 37 *The Journal of law, medicine & ethics : a journal of the American Society of Law, Medicine & Ethics* 369.

¹³⁹ Slokenberga (n 33) 1, 3, 4, 7, 8.

¹⁴⁰ Legislative observatory, *In vitro* diagnostic medical devices. European Parliament, [http://www.europarl.europa.eu/oeil/popups/ficheprocedure.do?reference=2012/0267\(COD\)&l=en#tab-0](http://www.europarl.europa.eu/oeil/popups/ficheprocedure.do?reference=2012/0267(COD)&l=en#tab-0), accessed 15 September 2016.

testing is getting increasingly affordable and easy to access; for example, a test for 40+ health conditions is available to consumers in European states for 169 EUR,¹⁴¹ or, for 380 EUR, to ascertain the risk of developing breast cancer.¹⁴² The companies have little, if any, control over who is purchasing the test and who is using them, particularly whether the user has reached the age of medical decision-making. Consequently, minors can not only purchase the tests and undergo the testing themselves, but they can also be subjected to testing by their legal guardians or caregivers, as direct-to-consumer genetic testing providers tend to accept requests to process samples taken from minors.¹⁴³ Given the method of contact between supplier and consumer, however, it is unclear what means a supplier has to (1) verify the origin of a cellular sample, (2) link the sample to the person alleged to be undergoing testing, and (3) confirm any legal authority that a purchaser has to order a test for another person, such as a child.¹⁴⁴

In addition to the areas of problems outlined above, offering a health-related service online allows easily undermining the national threshold for setting the legal age for consent to biomedical interventions or healthcare. Testing as such reflects a broader concern as regards what is known as servicification – taking what is normally a service and selling it as a good – providing uncontrolled access to care that is of questionable overall quality or utility, as well as uncertain medical necessity. As a result, questions remain whether the current practice of direct-to-consumer genetic testing is compliant with the protection afforded to minors as regards decision-making in healthcare generally, as well as whether the existing regulatory approaches are sufficient in responding to privacy challenges. On a more general level, similar questions remain as to whether the mechanisms in place are adequate to respond to the challenges that servicification brings, namely, that healthcare service is not provided through regulated healthcare personnel but through consumer-provider relationships in the sale of a good.

4.3 Next generation prenatal testing

4.3.1 Scientific background

For a considerable time, various medical advances have allowed pregnant women to access genetic information about their fetuses through such interventions as amniocentesis, chorionic villus sampling (CVS) and preimplantation genetic diagnosis, the latter of which is used in connection with assisted reproduction and examined in Chapter 3. Both amniocentesis and CVS require insertion of a needle, respectively, into the amniotic sac or placenta – an act which has been associated with miscarriage.¹⁴⁵ Potential injury to the fetus and future born child is difficult to observe for causal effects and therefore is poorly studied. Because of the invasive nature of the tests, many parents may be offered the analysis only in cases of rare disorders, particularly those involving trisomy conditions, such as Down's syndrome.

In response to many concerns of highly invasive testing, *non-invasive genetic testing* or *NIPT* has emerged as an alternative form of prenatal testing, using cell-free DNA circulating in maternal blood, a sample of which can be used for the test. It has been sold commercially as an attractive option for women to ascertain genetic risks relating to the fetus and conducted at an early stage of pregnancy, with potential for high accuracy.¹⁴⁶ As public health care systems are increasingly

¹⁴¹ 23andMe, <https://www.23andme.com/en-eu/>, accessed 15 September 2016.

¹⁴² DNA Care, <http://dna-care.com/produkt/brostdancer/>, accessed 5 January 2017.

¹⁴³ Pascal Borry and others, 'Direct-to-Consumer Genome Scanning Services. Also for Children?' (2009) 10 *Nature Reviews Genetics* 8.

¹⁴⁴ Slokenberga (n 33) 4, 8.

¹⁴⁵ Kliegman and others (n 14) 543–549.

¹⁴⁶ Mollie A Minear and others, 'Global Perspectives on Clinical Adoption of NIPT' (2015) 35 *Prenatal Diagnosis* 959. Non-invasive prenatal testing (NIPT) uses cell-free foetal DNA (cff DNA) to assess the risk of foetal trisomy 21, trisomy 18 and

considering its use, more studies involving NIPT have confirmed its potential for screening purposes, so far only for a narrow class of high-risk pregnancies.¹⁴⁷ Because many of these pregnancies are terminated, their validity for determining fetal or birth outcomes is quite limited.¹⁴⁸ Nevertheless, the reduced cost and non-invasive character have resulted in considerable advocacy in the medical literature for their increased usage.

4.3.2 Analysis

As NIPT is being carried out on a sample of maternal blood, the pregnant woman is subjected to the testing. In principle, however, the NIPT technology has the capacity to allow sequencing of the entire fetus's genome, allowing the prospective mother or parents to access the genetic make-up of their fetus before birth.¹⁴⁹ At least in the European context, this raises many of the aforementioned privacy concerns for future children, once those rights attach at birth.¹⁵⁰ Apart from the potential of unprecedented private information about the child to the parent, the child's right not to know information could also be at stake. This kind of an intervention, therefore, requires reconsidering genetic privacy and adequacy of the regulatory framework for genetic-related questions, specifically regarding minors, with unclear questions how proportional the access to information is for the benefit of the child.

4.4 Genomic sequencing of newborns

4.4.1 Scientific background

Sequencing of the genome, in whole or in part, to determine the order of the bases or nucleotides in an individual's DNA to obtain a more comprehensive genetic portrait of that individual. Its diagnostic potential is presumed to determine an array of risks of acquiring a medical condition in an individual. Much has been learned from the Human Genome Project and its counterparts that have improved the method for sequencing, though it currently remains costly for most individuals. As a result, whole genome sequencing (WGS) is considered less clinically practical than sequencing a portion of it – a process described as whole exome sequencing (WES). Despite the wealth of information that comes from WES, substantial clinical concern has been raised about overvaluing its utility, as no technological process is error free and the current degree of predictive value for an array of genetic traits is considerably variable; thus, many expert recommendations now urge that the testing itself should not be considered sufficiently diagnostic without further examinations, such as laboratory tests, to confirm any results or claims.¹⁵¹

Current research is underway regarding the possibilities to sequence a child's genome upon birth and apply it into clinical practice. A prominent manifestation of this research is the BabySeq

trisomy 13, with a greater sensitivity and specificity than conventional serum analyte screening tests. Ruth M Farrell and others, 'Online Direct-to-Consumer Messages about Non-Invasive Prenatal Genetic Testing' (2015) 1 *Reproductive Biomedicine & Society Online* 88.

¹⁴⁷ Lyn S Chitty and others, 'Uptake, Outcomes, and Costs of Implementing Non-Invasive Prenatal Testing for Down's Syndrome into NHS Maternity Care: Prospective Cohort Study in Eight Diverse Maternity Units' (2016) 354 *bmj* i3426. Diana W Bianchi and others, 'DNA Sequencing versus Standard Prenatal Aneuploidy Screening' (2014) 370 *New England Journal of Medicine* 799.

¹⁴⁸ Glenn E Palomaki and James E Haddow, 'Confusion between Analytic Validity and Clinical Validity' (2016) 215 *American Journal of Obstetrics & Gynecology* 533.

¹⁴⁹ Helen Thomson, 'Baby's Genes Mapped at Birth' (2015) 226 *New Scientist* 8.

¹⁵⁰ *Case Vo v France* [GC], App No 53924/00, 08 July 2004.

¹⁵¹ Gert Matthijs and others, 'Guidelines for Diagnostic next-Generation Sequencing' (2016) 24 *European Journal of Human Genetics* 2. Sue Richards and others, 'Standards and Guidelines for the Interpretation of Sequence Variants: A Joint Consensus Recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology' (2015) 17 *Genetics in Medicine* 405.

Project, the first clinical trial of its kind to involve WES of newborns.¹⁵² This project is scheduled to run from 2015-2018 and aims to examine how best to use genomics in clinical pediatric medicine by creating methods for safe use and integration of sequencing into the care of newborns, as well as to monitor the long-term impact of the genomic information that is returned to families, and examine how this information may be impacting a child's medical care.¹⁵³ It entails genomic sequencing of the newborns in order to detect gene variants that are linked to childhood-onset conditions. This may be an alternative to blood tests used to screen for approximately 30 heritable and treatable conditions. The genomic sequencing will allow for significantly more extensive screening of disorders that newborns could be at risk for developing during childhood, whereas assessment of the return of genomic information to the families will allow ascertaining whether there are any differences between families who receive the genomic information and between those families that receive the standard of care.¹⁵⁴

4.4.2 Analysis

As with other genetic tests, analysis of the human genome can be regarded as an intervention in an individual's private life. Therefore, it is essential to reconcile the possible benefits of genomic sequencing at early childhood with the protection of privacy. In the context of predictive information, accurate interpretation of the genetic information in light of the scientific progress is necessary. Likewise, the necessity of medical interventions needs to be monitored to safeguard the child's right to the highest attainable standard of health. Therefore, it is essential to examine whether, to what extent, and how this practice could be seen as relating to the child's right to the highest attainable standard of health.

Finally, these samples and data are valuable resources in research and clinical practice, as well as information could be important in health and non-health related issues. Such protections as security measures for the data and sample sets need to be considered in light of children's right to their data protection and privacy. Depending on how this information could further be used, effective protection from discrimination and the prevention of stigmatization based on human genome may be crucial.

4.5 Genome editing

4.5.1 Scientific background

New therapeutic genetic strategies are emerging to modify nucleic acids within disease-affected cells and tissues, with potential for treatment of monogenic, highly penetrant diseases, such as severe combined immunodeficiency, hemophilia, and certain enzyme deficiencies, due to their well-defined genetics and often a lack of safe, effective alternative treatments.¹⁵⁵ Currently, two technologies can be regarded as the most powerful in genome editing: gene therapy and RNA interference (RNAi). Gene therapy enables restoration of missing gene function by viral transgene expression. RNAi mediates targeted repression of defective genes by knockdown of the target mRNA.

Genome-editing-based therapy can be achieved through a number of approaches, including corrections or inactivation of deleterious mutations, introduction of protective mutations,

¹⁵² Project BabySeq, <http://www.genomes2people.org/babyseqproject/>, accessed 25 October 2016.

¹⁵³ The Baby Seq project David Benjamin Turitz Cox, Randall Jeffrey Platt and Feng Zhang, 'Therapeutic Genome Editing: Prospects and Challenges' (2015) 21 *Nature medicine* 121.

¹⁵⁴ *ibid.*

¹⁵⁵ The information from this section is drawn from Cox, Platt and Zhang (n 153).

addition of therapeutic transgenes, or disruption of viral DNA.¹⁵⁶ Depending on the technology that is being applied, a mutation may be able to be corrected – for example, to deactivate the mutant gene, recover a gene function, eliminate pathogenic activity, or confer novel functions that protect against diseases. The editing can be performed *ex vivo* and *in vivo*. *Ex vivo* editing entails removing the target cell population from the body, modified with programmable nuclei, which are then transplanted in the host. *In vivo* genome editing entails direct delivery of programmable nuclei to disease-affected cells in their native tissues. The technologies that enable editing the human genome are thus promising the possibility to achieve therapeutic genome-editing in disease cells and tissues, resulting in the removal or correction of deleterious mutations or the insertion of protective mutations.¹⁵⁷ However, they could also be used for non-medical purposes, such as genetic enhancement.

4.5.2 Analysis

Gene editing as a new technology holds considerable therapeutic potential.¹⁵⁸ However, it also mandates consideration of the circumstances under which gene editing should be regarded as safe and effective to apply in clinical practice, particularly for children. Among experts, no agreement has been reached on the threshold of when genome editing can be regarded as acceptably safe and effective.¹⁵⁹ In fact, experts have called for a moratorium on this technology, even for health-related purposes until the societal, environmental, and ethical issues can be discussed among stakeholders.¹⁶⁰

From a pure biomedical perspective, genome editing is a general process, with broader implications than those for which it may be intended in healthcare.¹⁶¹ Article 13 of the Convention on Human Rights and Biomedicine permits interventions that are aimed at modifying the human genome only for preventive, diagnostic or therapeutic purposes but not to introduce any modification in the genome of any descendants. It is essential, therefore, to assess the boundaries of such a provision as Article 13 to determine whether a line can clearly be drawn for such purposes.¹⁶² Indeed, there may be considerable difficulty in determining where a self-therapeutic purpose begins and ends, for example, to gather information to eradicate a genetic disorder or carrier gene that could be passed on to others – the search for which could cover a wide array of conditions and information.¹⁶³ As the understanding of human genes evolves, speculation over their significance, including the genetic link to intelligence and physical characteristics are coming to the fore. Even without regard to how the technology may be applied in clinical practice in the future, the broader implications for redesign of children may be on the horizon.

¹⁵⁶ *ibid.*

¹⁵⁷ *ibid.*

¹⁵⁸ Eric S Lander, 'Brave New Genome' (2015) 373 *New England Journal of Medicine* 5.

¹⁵⁹ Ignacio Anegón and Tuan H Nguyen, "'My Life Needs Editing'" (Mort Sahl) and 'Genome Editing Needs Ethics' (2016) 16 *Current gene therapy* 1.

¹⁶⁰ David Baltimore and others, 'A Prudent Path Forward for Genomic Engineering and Germline Gene Modification' (2015) 348 *Science* (New York, N.Y.) 36.

¹⁶¹ Donald B Kohn, Matthew H Porteus and Andrew M Scharenberg, 'Ethical and Regulatory Aspects of Genome Editing' (2016) 127 *Blood* 2553.

¹⁶² David DeGrazia, 'Enhancement Technologies and Human Identity 1' (2005) 30 *Journal of Medicine and Philosophy* 261. *Case Odièvre v France* [GC], App No 42326/98, 13 February 2003, para 29.

¹⁶³ Sigrid Sterckx and others, "'I Prefer a Child with ...': Designer Babies, Another Controversial Patent in the Arena of Direct-to-Consumer Genomics' (2013) 15 *Genetics in Medicine* 923. Masha Gessen, *Blood Matters: From BRCA1 to Designer Babies, How the World and I Found Ourselves in the Future of the Gene* (Houghton Mifflin Harcourt 2009). Bonnie Steinbock, 'Designer Babies: Choosing Our Children's Genes.'

4.6 Summary of the rights at stake

The developments in the area of genetics and genomics are considerable. They offer the possibilities to ascertain the risks of genetic conditions and treatment for them. However, the application of these advances in relation to children presents numerous of challenges. For each of the genetic testing services, the amount of private information collected about a child may be unlimited, which is why disregarding of the technology that is being used particularly informational dimension of privacy is at stake, with potential effects in several cases for other rights of the child, as set forth below.

Scientific challenge/procedure	Rights at stake
Genetic analysis: method of supply	<ul style="list-style-type: none">• Right to privacy
Non-invasive prenatal testing	<ul style="list-style-type: none">• Right to privacy
Genomic sequencing of newborns	<ul style="list-style-type: none">• Right to privacy• Right to family life
Genome editing	<ul style="list-style-type: none">• Right to personal identity



5. Clinical practices for children classified as minorities based on their gender, sexuality, and physical sex characteristics

5.1 Introduction

Historically, biomedicine has been a powerful locus of harm for lesbian, gay, bisexual, transgender, and intersex persons. When grouped together for public discourse, these persons are often referred to as “LGBTQI persons” (with “Q” for queer or questioning), even though the interests of the individuals so classified are quite different. Individuals in the class can, however, commonly trace the harms that they have endured in biomedicine to presumptions that all persons should look, behave, and identify in ways commonly associated with being a “typical” or “normal” male or female person – one who is presumed to be heterosexual or cisgender. In the past, medical experts have played a significant role as “experts” scrutinizing the sexuality and gender of individuals to resolve disputes about the rights of those who do not conform to social norms. Worldwide, clinicians today remain primarily responsible for registering a child as male or female, with significant social and legal consequences. In the last century, they have also developed a series of invasive physical and psychological interventions in order to “normalize” people with diverse genders, sexualities, and sex characteristics, often directed at children. Many of these practices have not faded into history, whereas a lack of equal access to patient-centered care persists in Europe for minorities defined by their gender and sexuality.

This chapter attempts to address the scientific challenges associated with clinical practices that affect children on the basis of sex characteristics, sexual orientation, and gender identity. Currently, many scholars recognize the difficulty of discourse on this topic because of a history of imposing identities and classifications on individuals based on discriminatory norms. Medically, this raises difficulties for children who have yet to identify as lesbian, gay, bisexual, transgender, or intersex and might never do so, but may need tailored health care – such as, among adults, the class clinically described as men who have sex with men (MSM), which is often said to include children as “young MSM”.¹⁶⁴ The medical literature also reflects a general recognition that diverse sexual orientations and gender identities are natural variations in human development, such that children who have experienced maltreatment as minorities are described as sexual or gender minority youth (SGM).¹⁶⁵ To reconcile these views, this chapter seeks to emphasize the importance of respect for the diverse identities of the persons concerned and reflects the medical literature’s general recognition that “sex” as a classifier only relates to physiological development and characteristics associated with it – casting “male” and “female” classifications as socially defined categories that reflect “gender”. Thus, the chapter addresses the persistence of *adverse care*, along with the lack of *access to care* that is supportive and nondiscriminatory for children defined socially and medically as sexual and gender minorities.

¹⁶⁴ See, e.g., ‘More than half of young HIV-infected Americans are not aware of their status’. Centers for Disease Control and Prevention, http://www.cdc.gov/media/releases/2012/p1127_young_HIV.html, accessed 19 November 2016.

¹⁶⁵ See, e.g., Kimberly H McManama O’Brien and others, ‘Sexual and Gender Minority Youth Suicide: Understanding Subgroup Differences to Inform Interventions’ (2016) 3 *LGBT Health* 248. Kathryn Macapagal and others, ‘“I Won’t Out Myself Just to Do a Survey”: Sexual and Gender Minority Adolescents’ Perspectives on the Risks and Benefits of Sex Research’ [2016] *Archives of Sexual Behavior* 1.

5.2 Children with differences in sex development and intersex conditions

5.2.1 Scientific background

For the last six decades, non-consensual gender assignment surgeries and other gender-“normalizing” treatments have been performed on tens of thousands of infants and young children – most frequently, those children diagnosed as having “intersex conditions” or a “disorder of sex development”, the latter term which is increasingly described as “differences in sex development”.¹⁶⁶ Since the 1990s, individuals who have been harmed by these practices have come forward reporting genital dysfunction, scarring, loss of sexual feeling, loss of fertility, chronic pain, and the wrong gender assignment – with irreversible excision of genital and gonadal tissues.¹⁶⁷ Despite clinical attempts to find data supporting these practices, repeated systematic reviews of evidence have found no quality data confirming their safety and benefits for each affected child.¹⁶⁸ Many prominent European clinicians remain among the most aggressive defenders of these practices – typically based on questionable studies tainted by views of what is best for the children and the ability of parents to “accept” a treatment recommendation, despite acknowledging the vast array of uncertainty surrounding the interventions in question.¹⁶⁹

The affected children are diagnosed for possible intervention to “normalize” their bodies when their differences in development are considered atypical for their genetic sex, or because they were born with sex characteristics that clinicians have considered difficult to fit into medico-legal classifications of what is “male” or “female”. Many have more complex development – some with genetic markers that are neither clearly XY nor XX, while others have atypical reproductive organs or gonads. For some, their sex development also changes atypically in puberty. Other children classified as having “DSD” or “intersex” conditions have minor variations in their sex development and grow to identify as male or female, regardless of any medical intervention.¹⁷⁰ Thus, a diversity of views has arisen as to how the bodies and identities of these children should be described as a class, which remains a source of considerable controversy.¹⁷¹ All of the children are grouped diagnostically based on their physical development and appearance relative to what is “typical” for medically defined “male” and “female” infants, without respect for the free development of their personalities or their future possible gender identities.

¹⁶⁶ Peter A Lee and others, ‘Global Disorders of Sex Development Update since 2006: Perceptions, Approach and Care’ (2016) 85 *Hormone Research in Paediatrics* 158.

¹⁶⁷ See National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases Research (NDDKR), *Strategic Plan for Pediatric Urology* (2006), 53-54. Consortium on the Management of Disorders of Sexual Development, *Clinical Guidelines for the Management of Disorders of Sexual Development in Childhood* (2006), 28.

¹⁶⁸ For a summary, see Lee and others (n 166).

¹⁶⁹ P Mouriquand and others, ‘The ESPU/SPU Standpoint on the Surgical Management of Disorders of Sex Development (DSD)’ (2014) 10 *Journal of Pediatric Urology* 8. See also, A Binet and others, ‘Should We Question Early Feminizing Genitoplasty for Patients with Congenital Adrenal Hyperplasia and XX Karyotype?’ (2016) 51 *Journal of Pediatric Surgery* 465. Ricardo González and Barbara Magda Ludwikowski, ‘Should the Genitoplasty of Girls with CAH Be Done in One or Two Stages?’ (2014) 1 *Frontiers in Pediatrics* 1. Arianna Lesma and others, ‘Sexual Function in Adult Life Following Passerini-Glazel Feminizing Genitoplasty in Patients with Congenital Adrenal Hyperplasia’ (2014) 191 *The Journal of Urology* 206.

¹⁷⁰ Indeed, the two most frequent conditions in this category include (1) *hypospadias*, in which the urethral opening is atypically located on the child’s penis or may be combined with other differences in sex development, and (2) various virilizing conditions in genetically female children that may result in a clitoris that is slightly to substantially larger than is typical for other female children.

¹⁷¹ See Tove Lundberg and others, ‘“It’s Part of Me, Not All of Me’: Young Women’s Experiences of Receiving a Diagnosis Related to Diverse Sex Development’ (2016) 29 *Journal of Pediatric and Adolescent Gynecology* 338. Martine Cools and others, ‘Response to the Council of Europe Human Rights Commissioner’s Issue Paper on Human Rights and Intersex People’ [2016] *European urology*. See also Elizabeth Reis, ‘Divergence or Disorder?: The Politics of Naming Intersex’ (2007) 50 *Perspectives in Biology and Medicine* 535.

Significantly, all evidence-based reviews concur that gender identity and sexual orientation of children with differences in sex development cannot be predicted with accuracy.¹⁷² As such, the high rates of rejection of gender assignment by surgically altered children are strong indicators of how poor clinical understanding of their actual gender development is.¹⁷³ Classifying these children as transgender relative to their juridical sex is problematic. Rather, their identities as male, female, a combination of both, or other identities such as “intersex” all can be consistent with some aspect of their sex development, such that their registered gender may be wrong. While most individuals affected by these gender-“normalizing” interventions appear to identify as male or female, research indicates that significant percentages are unsatisfied with their gender assignment and have a complex gender identity.¹⁷⁴ Because gender assignment affects how one’s sexuality is viewed socially, surgical intervention may also impose a sexual classification on these children.¹⁷⁵ Currently, the medical literature has not addressed the implications of whether clinicians and parents have a right to assign these identities surgically and irreversibly on children.

Scientific uncertainty in the advancement of treatment protocols

The history of gender-“normalizing” treatment protocols is often oversimplified, but it is critical to an understanding of the persistence of the interventions in question.¹⁷⁶ Both in Europe and the US, the roots of surgical intervention on children derived from disagreement over what characteristics should determine a male or female assignment for a child with complex sex development. The medical literature also reveals clinical anxiety that children with atypical genital appearance would suffer stigma, social discrimination, sexual frustration, and, of most significance, rejection by their parents. It also reflects considerable hostility to perceived homosexuality in patients that clinicians believed were living in the “wrong” gender. The surgical practice had evolved from experience with patients with differences in sex development who had sought surgery consistent with their gender identity. By the 1940s, these surgeries were increasingly performed by clinicians on older children at the request of the children’s parents. In response, researchers at Johns Hopkins University performed psychological studies of patients raised without surgery in childhood, to determine whether their mental health was impaired by living with their differences. Their findings confirmed that these individuals overall showed no signs of psychological “nonhealthiness”, despite suffering stigma and social rejection.¹⁷⁷ However, the researchers also noted that children over age three who were surgically altered at parental request showed severe signs of psychological trauma, particularly when the gender chosen by clinicians and parents was contrary to the identities that the children had begun to express. For all of these reasons, the protocols that emerged from this period determined that surgery should be done in infancy on the assumption that parental rearing could steer gender development.

The treatment protocols that emerged from the US-based recommendations were not based on any clinical trials or careful research. Rather, they had three theoretical ambitions: *first*, to support a preferred gender assignment, determined in part based on whether medical interventions could

¹⁷² Garland (n 6) 108, 110–112.

¹⁷³ *ibid* 108–110, 117–121.

¹⁷⁴ Katinka Schweizer and others, ‘Gender Experience and Satisfaction with Gender Allocation in Adults with Diverse Intersex Conditions (divergences of Sex Development, DSD)’ (2014) 5 *Psychology & Sexuality* 56.

¹⁷⁵ Garland (n 37) 110–112.

¹⁷⁶ Many European reports attribute the origin of these procedures to the US, and particularly individual clinicians, without accounting for the responsibility of their own clinicians and health systems to scientifically validate care. *See* *ibid* 51–93. For more complex accounts, *see* Sandra Eder, ‘From “following the push of Nature” to “restoring one’s proper sex” – cortisone and Sex at Johns Hopkins’s Pediatric Endocrinology Clinic’ (2012) 36 *Endeavour* 69. Elizabeth Reis, *Bodies in Doubt: An American History of Intersex* (Johns Hopkins University Press 2009).

¹⁷⁷ John Money, Joan G Hampson and John L Hampson, ‘Sexual Incongruities and Psychopathology: The Evidence of Human Hermaphroditism’ (1956) 98 *Bulletin of the Johns Hopkins Hospital* 43. Joan G Hampson, ‘Hermaphroditic Genital Appearance, Rearing and Eroticism in Hyperadrenocorticism’ (1955) 96 *Bulletin of the Johns Hopkins Hospital* 265.

feasibly reconstruct a typical body for the assigned gender; *second*, to enable “penile-vaginal intercourse”, as the default and presumed preference for sexual activity; and *third*, to reduce anxiety among children about their atypical appearance, in part on the theory that such anxiety would lead to gender confusion.¹⁷⁸ The emerging paradigm resulted in what is now called a “bias toward feminization”, on the assumption that children with female reproductive organs should be feminized to enable motherhood, but that “inadequate males” and children with mixed sex characteristics should be feminized if expected to suffer embarrassment as males, difficulty in urinating standing, and having penetration difficulties in sex.¹⁷⁹ The goal of enabling “penile-vaginal” intercourse has also reflected a heterosexual preference for the child sexually without regard to the child’s actual sexual orientation or desires.¹⁸⁰

Understanding the peculiar scientific method behind these protocols is essential to understanding the persistence of the interventions in question. Until the end of the 20th century, the protocols were implemented in practice without any long-term data or follow-up confirming their safety and benefit to patients. As the first surgeon to come forward documenting gender assignment rejection by surgically altered children has explained, “Clinicians, seduced mostly through a sense of helplessness in caring for these children, unwittingly conducted what were in essence experiments, as though looking for data to fit the model”, which – once confronted with evidence of harm and significant scientific error – left practice in a state of “decision-making paralysis”, “entrenchment”, and “clinical confusion”.¹⁸¹ Thus, despite considerable evidence of the harms done and uncertainty in going forward, the traditional protocols have only been modified: *first* to use the limited medical literature and detailed genetic analysis to attempt to predict the child’s gender with more caution, and *second*, to attempt new surgical techniques to spare loss of sensitivity and other harms due to reconstructive and cosmetic surgeries.

The most commonly referenced version of these protocols, known as the Chicago Consensus, recommended the delay of some procedures (such as vaginoplasty) but left parents to decide others.¹⁸² Audits in Europe indicate that even these recommendations may not be widely followed.¹⁸³ The European Society of Pediatric Urology has formally objected to human rights criticism and has favored continuing modified practice, conceding that delaying procedures for the child’s consent may be wise, but also making delay dependent on parents’ expectations.¹⁸⁴ So far, only one international protocol, by the Consortium on the Management of DSD, has recognized that consent of the child is necessary to ensure that any interventions coincide with the child’s wishes. Few clinicians have publicly endorsed that protocol. No other protocol has emerged to explain, as a matter of science, how infant surgery will be certain to coincide with the child’s actual identity, sexual interests, and desires for bodily appearance.¹⁸⁵

¹⁷⁸ William Byne and others, ‘Report of the American Psychiatric Association Task Force on Treatment of Gender Identity Disorder’ (2012) 41 Archives of Sexual Behavior 759, 789.

¹⁷⁹ Garland (n 6) 5–7, 94–125.

¹⁸⁰ Byne and others (n 178) 789.

¹⁸¹ William Reiner, ‘Prenatal Gender Imprinting and Medical Decision-Making: Genetic Male Neonates with Severely Inadequate Penises’ in Sharon Preves (ed), *Ethics and Intersex* (Springer 2005) 159.

¹⁸² Ieuan A Hughes and others, ‘Consensus Statement on Management of Intersex Disorders’ (2006) 2 Journal of Pediatric Urology 148, 158.

¹⁸³ Garland (n 6) 9, 94–95, 110–112.

¹⁸⁴ Pierre Mouriquand and others, ‘The ESPU/SPU Standpoint on the Surgical Management of Disorders of Sex Development (DSD)’ (2014) 10 Journal of Pediatric Urology 8.

¹⁸⁵ Milton Diamond and Jameson Garland, ‘Evidence Regarding Cosmetic and Medically Unnecessary Surgery on Infants’ (2014) 10 Journal of Pediatric Urology 2.

Since 2006, several reviews of evidence by clinician-researchers have been conducted to determine whether gender “normalizing” treatments are safe and beneficial for children with differences in sex development and intersex conditions. The first of these reviews was conducted by a gathering of fifty of the world’s leading practitioners in Annecy, France (the Annecy Working Party), which concluded that long-term studies about the safety and efficacy of these treatments do not exist, and that even the best studies “lack the necessary detail to base further recommendations” on future care for individual children.¹⁸⁶ Addressing the timing of gender conforming surgery in infancy, the Working Party further warned that (1) “quality of life” studies on patients into adulthood are lacking and are “poorly researched”, (2) the overall impact on the sexual function on children surgically altered is “impaired” and (3) the claim that gender development requires surgery is a “belief” unsubstantiated by data.¹⁸⁷ A second review from the American Psychiatric Association (APA) Task Force similarly reported that the quality of evidence was so low that it was “difficult to draw conclusions sufficient for evidence-based recommendations”, describing current treatment guidelines as “uncomfortably nonspecific”.¹⁸⁸ The most recent review, published in 2016, concluded that there is no consensus among expert practitioners as to the need, timing, safety, or efficacy of these procedures.¹⁸⁹

Currently, all evidence-based reviews acknowledge that harms have occurred and may continue to occur for patients, including pain, dysfunction, error in gender assignment, and harm to their quality of life. On the scientific question of whether intervention is *necessary*, only three medical procedures have been identified as meeting that criteria in some infants: (1) administration of endocrine treatment to prevent fatal salt-loss in some infants, (2) early removal of streak gonads in children with gonadal dysgenesis, and (3) surgery in rare cases to allow exstrophic conditions in which organs protrude from the abdominal wall or impair excretion.¹⁹⁰ Cancer risks to children with undescended testicles in most cases do not require gonad removal in infancy and can be delayed until late puberty or early adolescence in some cases, or even into adulthood. Older children with the need to menstruate may require surgical intervention to prevent vaginal pooling and other related harms, but an adolescent in such circumstances might prefer facilitation of a male gender assignment rather than vaginoplasty or may prefer temporary measures to facilitate menstruation without such procedures. None of the aforementioned reviews have identified any other procedure as medically necessary or confirmed to have a balance of long-term benefits from gender-“normalizing” interventions in infancy.

5.2.2 Analysis

As of 2016, eight international human rights authorities – three from the United Nations¹⁹¹ two each from the Council of Europe¹⁹² and European Union¹⁹³ and one from the Organization of

¹⁸⁶ Peter Lee and others, ‘Review of Recent Outcome Data of Disorders of Sex Development (DSD): Emphasis on Surgical and Sexual Outcomes’ (2012) 8 *Journal of Pediatric Urology* 611.

¹⁸⁷ See Sarah Creighton and others, ‘Timing and Nature of Reconstructive Surgery for Disorders of Sex Development - Introduction’ (2012) 8 *Journal of Pediatric Urology* 602. Justine Schober and others, ‘Disorders of Sex Development: Summaries of Long-Term Outcome Studies’ (2012) 8 *Journal of Pediatric Urology* 616.

¹⁸⁸ Byne and others (n 178) 789.

¹⁸⁹ Lee and others (n 166).

¹⁹⁰ Garland (n 6) 110–115, 269–270.

¹⁹¹ The UN’s High Commissioner for Human Rights, WHO, and Special Rapporteur for Torture and Degrading Treatment have all issued recommendations, see United Nations High Commissioner for Human Rights, *Discrimination and violence against individuals based on their sexual orientation and gender identity* (2015). WHO, *Eliminating forced, coercive and otherwise involuntary sterilization: An interagency statement* (May 2014). Juan E. Méndez, Report of the special rapporteur on torture and other cruel, inhuman or degrading treatment or punishment to the U.N. General Assembly, 2013 (A/HRC/22/53), paras 77, 88.

¹⁹² Council of Europe Commissioner for Human Rights, *Human rights and intersex people*. Issue Paper CommDH/IssuePaper (2015)1. Council of Europe Parliamentary Assembly, Resolution 1952 (2013) *Children’s right to physical integrity*.

American States¹⁹⁴ – have called on all nations to either “repeal laws” that permit these procedures or “take measures” to prohibit gender-normalizing treatments that are not necessary for the physical health of the child without the child’s free and informed consent. Several UN Committees have also made specific recommendations to individual nations to stop nonconsensual procedures on intersex persons, including the Committee on the Rights of the Child (“medically unnecessary” treatments), the Committee Against Torture (“non-urgent” treatments) and the Committee on the Rights of Persons with Disabilities (“irreversible” procedures).¹⁹⁵ As of October 2016, Austria, Denmark, France, Germany, Ireland, Italy, Switzerland, and the United Kingdom have all been specifically directed to take such actions. To date, Malta is the only European nation to do so (and without specific direction).

Though *the right to consent* is the touchstone of these recommendations, several other rights are clearly intended to be protected in part through consent, including: (1) *the right to physical and psychological integrity*, which is undermined by invasive and injurious procedures; (2) *the right to private life* in intimate matters and identity, which many authorities recognize as inclusive of gender and sexual identity as well as privacy regarding intimate sexual activity; (3) *the right to information*, both for children who may choose or refuse these treatments and their parents in managing their care; (4) the freedom from *torture, inhuman and degrading treatment*, including medical abuse related to all aspects of surgery, hormonal treatments, and aftercare; (5) *the right to the highest attainable standard of health*, which should also be paired with *freedom from experimentation*; as children continue to undergo unproven treatments without proof of their therapeutic character; and finally, but significantly (6) *the right of the child to be heard* in matters affecting the child. This last right remains the central right critical to requiring a delay of any procedures until the child can give the input necessary to ensure that the interventions match the child’s gender, sexual interests, and other wishes for their bodies. Parental consent is inherently problematic as there is no credible evidence that children benefit from improved attachment with parents who want these interventions. Indeed, parental desire for the interventions complicates the eventual transfer of control over to the children for their own gender and sexuality, which then becomes difficult for parents and clinicians who find their children’s own decisions to be unconventional.¹⁹⁶

The current recommendations vary significantly in limiting proposed restrictions to “medically unnecessary” and “non-urgent” treatments, raising questions about how governments and health care professionals will implement them.¹⁹⁷ Cancer risk has been used to classify undescended testicle removal as a medical necessity, but the timing of the procedure remains a problem, especially if fertility preservation options are not offered to the child. Even with the delay of the procedure until the child can fully consent, changes in health care protocols will be required, with increased monitoring and care for the child and guarantees that fertility options are preserved. Many other procedures are also rigorously defended by clinicians as highly beneficial to the health of the child and thus “necessary” for healthy functioning, such as hypospadias repair to enable “normal” urination in boys and vaginal-urethral separation in girls to prevent urinary tract infections – neither of which are supported by quality evidence of safety, benefit, or necessity and both of which risk irreversible injury. In other cases, for children whose parents have already

¹⁹³ EU Agency for Fundamental Rights, *The fundamental rights situation of intersex people* (2015). Council of the European Union, *Guidelines to Promote and Protect the Enjoyment of All Human Rights by Lesbian, Gay, Bisexual, Transgender and Intersex (LGBTI) Persons* (2013).

¹⁹⁴ Comisión Interamericana de Derechos Humanos, *Organización de los Estados Americanos, Violencia contra Personas Lesbianas, Gays, Bisexuales, Trans e Intersex en América*, OAS/Ser.L/V/II.rev.1, Doc. 36 (2015).

¹⁹⁵ Garland (n 6) 108, 110–112.

¹⁹⁶ Justine Schober and others, ‘Disorders of Sex Development: Summaries of Long-Term Outcome Studies’ (2012) 8 *Journal of Pediatric Urology* 616, 617.

¹⁹⁷ The specific language of these recommendations varies significantly relative to the medical science. The UN Special Rapporteur, for example, directed its recommendations toward “intrusive and irreversible treatments, including forced genital-normalizing surgery, involuntary sterilization, unethical experimentation” whereas the Parliamentary Assembly of the Council of Europe focused its recommendation on “unnecessary medical or surgical treatment that is cosmetic rather than vital for health during infancy”. For a discussion of how these directives are complicated medically, see Garland (n 6) 108, 110–112.

consented to vaginoplasty, a post-operative ban on medical procedures may not cover continued parental dilation of the child's vagina to "maintain" it if was surgically constructed before the ban. Dilation, requiring parents or clinicians using a tool or finger to penetrate the vagina on young children who cannot perform the procedure, has caused severe psychological trauma to many children who have endured repeated vaginal penetration without their consent.

The shift to respect for the right of the child to consent to any gender-related procedures will also likely require reformulations of legal rules to guarantee all rights associated with health care, bodily integrity, and gender identity. *First*, treatment protocols will need to be better developed to ensure access to the highest attainable standard of care for children with differences in sex development and intersex conditions who want treatments supporting them in their gender identity, even at odds with the wishes of their parents. *Second*, medico-legal procedures for juridical gender registration will likely require protections for children who identify as intersex or to delay registration to permit the child to choose a gender in accordance with the child's identity. In these and other areas, the child may also require enhanced legal protections from discrimination in health care, in schools, and even, potentially, from their parents.

5.3 Clinical efforts to "change" sexual orientation and gender identity

5.3.1 Scientific background

Homosexuality and gender nonconformity were pathologized by psychiatry in the mid-1800s, reaching a peak in the 1900s, with medical efforts to change or suppress sexual desire and behavior with invasive interventions such as lobotomies, shock therapy, chemical castration, and induced vomiting.¹⁹⁸ The WHO has warned that health care professionals have also engaged in coerced genital and anal examinations of persons suspected of being gay and lesbian, and, in some parts of the world, continue to sterilize such persons.¹⁹⁹ While these treatments are no longer considered prevalent in much of Europe, compulsory psychotherapy on lesbian, gay, bisexual, and transgender children, sought by their parents, has not been formally outlawed in most jurisdictions. As the EU Agency for Fundamental Rights recently reported, clinicians in many European nations continue to consider homosexuality and variance in gender identity as "pathologies", the diagnoses of which are still included in training materials.²⁰⁰

Most professional psychiatric and psychological organizations in Europe and North America acknowledge that homosexuality is not a disorder and that there is no credible evidence that sexual orientation can be changed.²⁰¹ For transgender persons, however, pathologization is still endorsed widely. As of July 2016, Transgender Europe reported that 36 European nations still required transgender persons who wish to change their registered gender to receive a diagnosis that their need is due to a mental disorder, while 30 still required medical treatment for such gender recognition and 23 required sterilization for the same.²⁰² The DSM-V and the ICD-10 describe identification with a gender other than the one assigned at birth and suffering associated with it as a medical disorder; the DSM-V describes it as *gender dysphoria* but still classifies it as a mental health disorder. The ICD-10 refers to it as a *gender identity disorder*, but a Working Group for ICD-11, which is anticipated in 2018, has proposed a new diagnostic term of "*gender*

¹⁹⁸ See Katz Jonathan, *Gay American History* (New York, Avon Books 1976). Garland (n 6) 295, 453.

¹⁹⁹ WHO, Sexual Health, Human Rights and the Law (2015), 23-24.

²⁰⁰ EU Agency for Fundamental Rights, Professionally speaking: challenges to achieving equality for LGBT people (2016), 63.

²⁰¹ Geoffrey M Reed and others, 'Disorders Related to Sexuality and Gender Identity in the ICD-11: Revising the ICD-10 Classification Based on Current Scientific Evidence, Best Clinical Practices, and Human Rights Considerations' (2016) 15 World Psychiatry 205. American Psychological Association Task Force, Appropriate Therapeutic Responses to Sexual Orientation (2009). Byne and others (n 178) 771.

²⁰² See Transgender Europe, the Transgender Rights Europe Index 2016 (2016). TGEU, http://tgeu.org/trans-rights_europe_map_2016/, accessed 20 November 2016.

incongruence” for children and adults, removing it from classification as a disorder.²⁰³ The WHO Working Group and the American Psychiatric Association both maintain that a diagnosis of some kind is necessary to ensure access to hormonal and surgical treatment for those who seek it.²⁰⁴ The World Professional Association for Transgender Health (WPATH) has found no evidence to treat nonconformity with gender assignment as a medical condition that can be changed but instead supports gender-affirming care.²⁰⁵

5.3.2 Analysis

Clinical efforts to change sexual orientation and gender identity raise many of the same concerns of medical abuse as do gender “normalizing” treatments on children with differences in sex development or intersex conditions, as reflected in the Yogyakarta Principles. The same rights – including the *freedom from torture, degrading and inhumane treatment* and the *right to physical and psychological integrity* – are implicated in this context as well. While there is considerable evidence that invasive conversion therapy has declined, the ratification of physical violations by states policing legal gender change are considerable, as transgender persons are often forced to seek medical examinations and in some jurisdictions “treatment” or sterilization in exchange for gender recognition. When youth are pressured or forced to undergo change efforts for sexual orientation or gender identity, it can also deeply affect their *right to be heard* and *the right to consent* in the expression and development of their *right to their identity*. Even without evidence of a lack of therapeutic value and intentional clinical bias, such therapies are directed only at lesbian, gay, bisexual and transgender children, and per se abrogate *the freedom from discrimination*. Government ratification of any gender identity as a disorder escalates these abuses to the status of law, much as a lack of protection of all of the affected children remains a serious concern if *the highest attainable standard of health* is taken seriously as a right.

5.4 Access to care for lesbian, gay, bisexual and transgender youth

5.4.1 Scientific background

Some reports about the lack of access to care for lesbian, gay, bisexual, and transgender persons, in general, have addressed the impact that discrimination has had on preventing the development of quality and supportive care. As clinical practice itself ideally advances, however, scientific uncertainty remains in how practice addresses the needs of sexual and gender minority children, particularly as the needs of these children are diverse,²⁰⁶ even though their needs sometimes overlap and create difficulties for helping children who have not come to terms with their identity or sexuality. The majority of young children who have been diagnosed with gender-related stress (clinically described as potential *dysphoria*) do not appear to go on to seek hormonal or surgical care to support a male or female identity; some of these children later identify as gay,²⁰⁷ while many live as transgender or a non-binary identity without any clinical treatment.²⁰⁸ Older children may be especially sensitive to a lack of inclusive care from clinicians presuming they are heterosexual and cisgender. All gender and sexual minority children are at higher risk of suicide, particularly those that lack supportive families.²⁰⁹ All gender and sexual minorities, furthermore,

²⁰³ Reed and others (n 201).

²⁰⁴ *ibid.* Byne and others (n 178) 768.

²⁰⁵ WPATH, Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People (2011).

²⁰⁶ Byne and others (n 178) 760–763.

²⁰⁷ *ibid.* Reed and others (n 201) 211.

²⁰⁸ Madeline B Deutsch, ‘Making It Count: Improving Estimates of the Size of Transgender and Gender Nonconforming Populations’ (2016) 3 LGBT Health 181.

²⁰⁹ Kimberly H McManama O’Brien and others, ‘Sexual and Gender Minority Youth Suicide: Understanding Subgroup Differences to Inform Interventions’ (2016) 3 LGBT health 248.

may be harmed by the lack of resources devoted to evidence-based clinical practice, particularly when innovative therapies are concerned.

Lesbian, gay and bisexual youth

Though many of the higher health risks facing lesbian, gay, and bisexual people are associated with the effects of societal discrimination, clinicians concerned with evidence-based preventive care have documented several risks warranting special attention to ensure optimal health for lesbian, bisexual, and gay youth. For example, clinicians are urged to be sensitive to potential risks for lesbian and bisexual girls and women, warranting preventive care, including:

- ❖ higher rates of breast cancer in adulthood, possibly related to lower rates of pregnancy and breastfeeding but requiring increased monitoring as precautions,²¹⁰
- ❖ higher rates of obesity and binge-eating²¹¹, for reasons not well understood, and
- ❖ higher risks of bacterial vaginosis, but not other sexually transmitted diseases (STD).²¹²

Similarly, for gay and male youth, clinicians need to be sensitive to the potential for risks among some youth, with attendant preventive care measures required, in specific areas:

- ❖ higher rates of body image problems, including eating disorders²¹³ and in some cases, potential for steroid abuse,²¹⁴
- ❖ exposure to certain STDs among sexually active youth, requiring specific preventive measures, such as a hepatitis vaccine, and
- ❖ risks of oral and anal cancer,²¹⁵ particularly associated with Human Papillomavirus (HPV) also favoring vaccination.

Eliminating discrimination and lack of training among clinicians is thus only the beginning of ensuring that care is based on high quality risk assessments for the affected youth.

In innovative care practices, the most controversial recent preventive measure currently proposed for gay and bisexual male youth is pre-exposure prophylaxis (PrEP). PrEP is medication for which early studies contain claims of prevention of HIV transmission from 90% to 98% in sexual encounters, depending on how frequently PrEP is taken each week.²¹⁶ Much of the evidence in the studies is circumstantial, based on patients who have remained HIV-negative after treatment, not based on documented unprotected sex between discordant partners with proof of non-

²¹⁰ Lesbian and Bisexual Health. Department of Health & Human Services, <https://www.womenshealth.gov/files/assets/docs/fact-sheets/lesbian-bisexual-health.pdf>, accessed 20 November 2016.

²¹¹ Bryn S. Austin and others, 'Sexual Orientation Disparities in Purging and Binge Eating from Early to Late Adolescence' (2009) 45 *Journal of Adolescent Health* 238.

²¹² Lesbian and Bisexual Health (n 210) 4.

²¹³ Bryn S Austin and others, 'Sexual Orientation, Weight Concerns, and Eating-Disordered Behaviors in Adolescent Girls and Boys' (2004) 43 *Journal of the American Academy of Child & Adolescent Psychiatry* 1115. Patricia L Kaminski and others, 'Body Image, Eating Behaviors, and Attitudes toward Exercise among Gay and Straight Men' (2005) 6 *Eating Behaviors* 179.

²¹⁴ Aaron J Blashill and Steven A Safren, 'Sexual Orientation and Anabolic-Androgenic Steroids in US Adolescent Boys' (2014) 133 *Pediatrics* 469. Z Mor and others, 'Gym Exercising Patterns, Lifestyle and High-Risk Sexual Behaviour in Men Who Have Sex with Men and in Heterosexual Men' (2014) 4 *BMJ* open e005205.

²¹⁵ Eric A Fenkl and others, 'HPV and Anal Cancer Knowledge Among HIV-Infected and Non-Infected Men Who Have Sex with Men' (2016) 3 *LGBT health* 42.

²¹⁶ Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 A Clinical Practice Guideline U.S. Public Health Service, <http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf>, accessed 20 November 2016.

transmission. In 2016, the European Medical Products Agency approved its use in the clinical market, without age restrictions, unless covered by national laws.²¹⁷

The original guidelines encouraged PrEP for men who engage in anonymous sex with men without a condom, but also encouraged those who take PrEP, however, to still use condoms. Because adults taking PrEP have tended not to use condoms, data shows that men taking PrEP are now contracting other STDs, such as syphilis and HPV, at accelerated rates.²¹⁸ The scientific data on the success of the use of PrEP by gay and bisexual youth is virtually non-existent. Taking PrEP regularly at least four times a week is essential to yield higher HIV protection, whereas access to supply and potential for adherence to the best regimen remain uncertain in youth.²¹⁹ Of most importance, adolescents have not been studied in clinical trials for the effect of PrEP on bone density and other toxicities, which have been found in adults.²²⁰

Transgender youth

Transgender children and youth need access to specialized care just as many lesbian, gay and bisexual children and youth do – including encouragement of access to cancer screenings, education of prevention and treatment of STDs, and needs for mental health support. Indeed, many transgender youths cross-identify as gay and lesbian relative to their gender identity and may face risks impacting those groups. Transgender youth, however, have only begun to benefit from growing public acceptance and remain, among SGM youth, those with the highest risk of suicide, requiring care that is supportive as well as engaged.²²¹

Unlike lesbian, bisexual and gay youths, however, some transgender youths may find access to clinical settings particularly problematic as their health care needs may not be typical relative to their gender – for example, a male who needs access to pediatric or adolescent gynecology and who may later need screening for ovarian cancer. Some may also want specific treatments to support them in their gender but may be more gender-fluid than clinicians expect. Even supportive professional guidelines and clinicians acknowledge that treatment protocols often are based on false categorical notions that a transgender person is likely to want to live in the “other” gender and receive care accordingly.²²² WPATH currently acknowledges that many transgender persons do not want surgery or hormonal treatment, with proposed revisions to its guidelines anticipated to embrace concepts of gender fluidity, recognizing that many may choose to seek care for some parts of their bodies and not others and to be gender atypical.²²³ Clinicians in the Netherlands – who have the longest history in Europe of serving transgender adolescents with hormonal interventions – have also recently warned that transgender adolescents themselves are often more cautious than clinicians in deciding when and whether to undergo certain treatments.²²⁴

²¹⁷ Truvada. European Medicines Agency, http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000594/human_med_001113.jsp&mid=W0b01ac058001d124, accessed 20 November 2016.

²¹⁸ Noah Kojima, Dvora Joseph Davey and Jeffrey D Klausner, ‘Pre-Exposure Prophylaxis for HIV Infection and New Sexually Transmitted Infections among Men Who Have Sex with Men’ (2016) 30 AIDS 2251.

²¹⁹ Sybil Hosek and others, ‘An HIV Pre-Exposure Prophylaxis (PrEP) Demonstration Project and Safety Study for Young MSM.’ [2016] JAIDS Journal of Acquired Immune Deficiency Syndromes.

²²⁰ Preexposure Prophylaxis for the Prevention of HIV Infection in the United States (n 216) 43.

²²¹ O’Brien and others (n 165). Augustus Klein and Sarit A Golub, ‘Family Rejection as a Predictor of Suicide Attempts and Substance Misuse Among Transgender and Gender Nonconforming Adults’ (2016) 3 LGBT health 193.

²²² Britt Colebunders, Griet De Cuypere and Stan Monstrey, ‘New Criteria for Sex Reassignment Surgery: WPATH Standards of Care, Version 7, Revisited’ (2015) 16 International Journal of Transgenderism 222.

²²³ *ibid.* WPATH SOC-7 (n 205) 8-11.

²²⁴ Lieke Josephina Jeanne Johanna Vrouwenraets and others, ‘Perceptions of Sex, Gender, and Puberty Suppression: A Qualitative Analysis of Transgender Youth’ [2016] Archives of sexual behavior 1.

An increasingly utilized physical intervention for some transgender minors involves puberty suppressants or blockers, which serve two purposes.²²⁵ First, increasing evidence indicates that transgender individuals sometimes experience increased gender incongruence and stress when the body masculinizes or feminizes. For these children, puberty becomes a critical and traumatic psychological point in development when their gender identity may not only conflict with physical development but expose them to public ridicule. Puberty blockers may also facilitate more successful surgical outcomes if desired, as many pubertal changes in the body are difficult to reverse. Puberty blockers are reversible and can be stopped, allowing puberty to resume. Long-term negative effects have not been documented, though this outcome is supported primarily only by long-term studies in the Netherlands. However, European researchers, including those from the Netherlands, continue to acknowledge that the long-term data about the full effects of puberty blockers is limited; systematic interdisciplinary worldwide research is required to corroborate it.²²⁶ For those children who suffer severe gender incongruence and are at risk of lifelong trauma or suicide, the potential for severe harm from lack of access is currently difficult to weigh against unknown effects of suppressing physical adolescent development.

The age at which puberty blockers may be administered is not yet firm or consistent in guidelines. General guidelines have historically recommended that blockers may be provided as puberty begins after observation of sustained dysphoria. Today, however, use of puberty blockers can be timed at the very beginning of puberty and the threshold between middle childhood and earliest adolescence, because of early diagnoses of gender dysphoria and a lack of a lower age limit in the use of the blockers as treatment. Because clinicians who have used puberty blockers on children with differences in sex development and multiple forms of “precocious puberty” acknowledge uncertainty in their effects, continued long-term study of their effects for the benefit of transgender youth and future adults is needed to ensure that transgender children and youth have access to the highest attainable quality care.

Physical interventions are increasingly offered to adolescents to support them in their gender. Hormone treatments may begin in adolescence in some European nations in mid- or late adolescence. WPATH guidelines advise that these treatments must be carefully staged,²²⁷ as they are not without risks, the most serious of which in some cases include loss of fertility, weight gain, diabetes and increased cancer risk. Adult patients have also noted that many side effects are unpleasant (nausea, headaches, mood changes, loss of libido) but they endure them for relief from gender incongruence.²²⁸ Current international guidelines advise that the first stage of treatment should only include hormonal treatment where effects can be reversed, followed by a period of adjustment to living with their effects before moving toward less reversible hormone treatments and then possible surgery. As with all surgeries, risk and positive outcomes for gender-affirming surgery often turn on surgical techniques and individual patient characteristics. Other surgeries may require implants or other cosmetic modifications, some of which remain experimental, with varying risks and benefits. The available outcome data available indicates that patients who feel a strong need for surgery are significantly improved by undergoing such care. However, long-term data on the outcomes for interventions begun in youth do not yet exist.

²²⁵ WPATH SOC-7 (n 205) 11-18.

²²⁶ Lieke Josephina Jeanne Johanna Vrouwenraets and others, ‘Early Medical Treatment of Children and Adolescents with Gender Dysphoria: An Empirical Ethical Study’ (2015) 57 *Journal of Adolescent Health* 367. Fuss and others, ‘Gender dysphoria in children and adolescents: a review of recent research’ (2015) 28 *Current Opinions in Psychiatry* 430.

²²⁷ WPATH SOC-7 (n 205) 10-21. William Byne and others, ‘Report of the American Psychiatric Association Task Force on Treatment of Gender Identity Disorder’ (2012) 41 *Archives of Sexual Behavior* 759.

²²⁸ See Diana Tourjee, *Hormone Therapy is Lifesaving — But Why is No One Studying Its Long-Term Effects?* OUT, <http://www.out.com/out-exclusives/2016/9/20/hormone-therapy-lifesaving-why-no-one-studying-its-long-term-effects>, accessed 19 November 2016.

5.4.2 Analysis

Access to medical care for lesbian, gay, bisexual and transgender children remains entangled with a legacy of discriminatory practice, if not lack of supportive care and adequate training. As a result, the *highest attainable standard of health* for these children will remain compromised in general until training is both sensitive and patient-centered for each child, relative to potential needs that must be explored with each patient. The challenge for clinicians is great, for example, to be supportive of children with strong feelings of gender identity that does not correspond to their registered gender but with the recognition that many may grow and change – perhaps in ways that may be difficult for heterosexual and cisgender medical personnel to understand.²²⁹ Insensitive presumptions, as well as clinical queries perceived as condescending, may be threatening to lesbian, gay, bisexual, and transgender children. Specific risks facing the broader communities with which they may identify may also result in disproportionate adverse health conditions for these children. Sexually active youth may be at known risk of life-threatening STDs that can be averted in some cases with vaccines (HPV) and some cases not (HIV). Children without supportive families may particularly be at greater risk of suicide. The known higher risk of suicide, especially among transgender children, requires active, preventive care. As innovative treatments are developed and applied to youth in this category with the best of intentions, assurances must be made that experimental care is also safe and effective for youth and that all care is nondiscriminatory and supportive.

5.5 Summary of the rights at stake

Sexual and gender minority children are at risk of considerable human right violations connected to biomedicine. Indeed, it is difficult to perceive any other group of children who have been subjected to so many invasive, medically unnecessary treatments without their consent, with the primary goal of suppressing atypical gender, sexuality, and identity. Children across the spectrum of diverse gender identities, sexual orientations, and differences in their physical characteristics are lacking protections under many national laws and are not prioritized in health care – perceived as a relatively small percentage of the population. It is precisely these risks that not only undermine health-related rights of these children, but that give biomedicine a troubling legacy in the effects it may have on their lives.

Scientific challenge/procedure	Rights at stake
Gender "normalizing" interventions on children with differences in sex development and intersex traits	<ul style="list-style-type: none"> • Right to the highest attainable standard of health • Right to physical and psychological integrity • Right to participate in decisions affecting the child • Right to informed consent
Clinical practices to change gender identity or sexual orientation	<ul style="list-style-type: none"> • Freedom from experimentation • Freedom from discrimination • Freedom from torture and degrading treatment
Access to care for sexual and gender minority children	<ul style="list-style-type: none"> • Right to the highest attainable standard of health • Freedom from discrimination

²²⁹ William Byne, 'Regulations Restrict Practice of Conversion Therapy' (2016) 3 LGBT health 97.



6. Children diagnosed with serious physiological and psychological health needs

6.1 Introduction

Human rights authorities have repeatedly cautioned that some of the most serious human rights abuses in health care have come at the expense of vulnerable groups, such as disabled persons or those with serious mental health conditions, with children within these groups facing increased risk.²³⁰ To date, most of these concerns have not focused on the contested science on which many medical interventions on these children are based. Indeed, considerable medical risks may be taken with the health of these children, justified by the perceived severity of the diagnoses of their conditions or difficulties associated with them. In this light, concern for the rights of these children in biomedicine cannot simply focus on abusive treatments. Rather it should extend to treatments in clinical practice claimed or believed to benefit the children but without evidence of safety or efficacy, many of which are invasive for children with chronic illness, rare diseases, or common mental “disorders” and may impose pain and other physical and psychological harms.

The children addressed in this chapter are grouped for two reasons. First, the particular conditions of each group are associated with significant risk-taking in health care, whether through the use of scientifically questionable treatment in standard care or experimental treatment inside and outside clinical research. Second, the parents of children in these cases may have their own interests that affect their ability to make decisions in the children’s best interests, whether due to stress in dealing with critically ill children, difficulty in managing their children’s conditions, or even hopes for their children’s recovery. Thus, biomedical interventions designed for the children addressed in this chapter require scrutiny to determine what the evidence is of benefit and harm of treatment, even if only so that those seeking to protect the long-term interests at stake for the affected children can better assess the scientific uncertainties involved.

6.2 Children diagnosed with significant physical health needs

6.2.1 *Scientific background*

When children are diagnosed with serious physical health needs, the conditions that they suffer often cannot be easily treated or cured; correspondingly, they are frequently offered a variety of treatments undergoing modification and innovation, with outcomes that are difficult to project. Standard care may still lack considerable outcome data supporting safety and efficacy of treatment. Additionally, however, as summarized in Chapter 2, parents of children with chronic diseases and other serious conditions may themselves suffer from psychological problems and stresses in dealing with them, often affected by their own hopes for the children or even their biases toward them. When these conditions coincide, the challenges for clinicians and parents in making objective treatment decisions are often significant.

²³⁰ For a summary, see Special Rapporteur, Human Rights Council, The right of everyone to the enjoyment of the highest attainable standard of physical and mental health, A/64/272 (2009).

For many children with serious physical disabilities or health concerns, many treatments are designed as quality-of-life treatments, even though the balance of actual benefits to each child may be difficult to prove, as the emotional and psychological benefits for families plays a considerable role in advocating treatment. Some examples illustrate the problem:

- ❖ Growth suppression therapies have long been used on the grounds of claims for the psychological benefit of children, for example, to slow the growth of “tall girls” and stall “precocious puberty”, as explained in chapter 2. For children with *severe physical and cognitive disabilities*, some clinicians increasingly perform these therapies to stunt the growth of the children so that their parents will be better able to lift, carry, and physically manage them as they age.²³¹ Many of the treatments are endocrinological and designed to manipulate skeletal growth and prevent the child from growing an adult body. For some female children, hysterectomies and breast removal have also been performed. Pediatric endocrinology surveys indicate sharp disagreement among clinicians about the appropriateness of these procedures, with about half of those surveyed agreeing to requests by parents to perform them.²³² Considerable concern has been raised that these treatments are not occurring in clinical trials or under ethical review – with long-term side effects unknown – but solely on the exercise of clinical judgment and parental wishes. Currently, parents and clinicians together decide on unknown bases when to stop treatment, such as when the child experiences thrombosis, alterations in blood chemistry, or other bodily transformations (such as the development of breast tissue in boys). Other clinicians have raised concerns that these procedures are solely being managed without the aid of developmental specialists, psychological support for the parents and child, and long-term investigations into the quality of the life of the child after treatment.
- ❖ For children with *severe disabilities and shortened life spans*, such as children with *Trisomy-18 syndrome*, parents often request a range of surgeries, both in the hope of keeping them alive but also to alter the physical anomalies that might be altered in “normal” children (such as overlapping fingers, cleft palate, and “clubbed” foot). The result is often surgical intervention on children to an unusually high and cumulative degree.²³³ Because of the shortened or uncertain life spans of the children, reconstructive surgeries may expose the children to risks and pain without clear long-term benefit.²³⁴ Indeed, for children with Trisomy-18, the majority of children die in infancy, and few live past the first year of life, with even less reaching adulthood.²³⁵ As with many other treatments on children with physical anomalies, questions linger as to what degree the treatments benefit each child, as research on the quality of life of the children undergoing surgeries has not been done.²³⁶
- ❖ For *extremely or “morbidly” obese adolescents*, bariatric surgery is increasingly performed – both in clinical trials and in general practice – on the theory that effective weight loss treatment for

²³¹ For an overview, see Nikki Kerruish, ‘Growth Attenuation Therapy: Views of Parents of Children with Profound Cognitive Impairment’ (2016) 25 Cambridge Quarterly of Healthcare Ethics 70. David B Allen and others, ‘Growth-Attenuation Therapy: Principles for Practice’ (2009) 123 Pediatrics 1556. Erik Parens, ‘Respecting Children with Disabilities—and Their Parents’ (2009) 39 Hastings center report 22. Should Parents of Children With Severe Disabilities Be Allowed to Stop Their Growth? NY Times, http://www.nytimes.com/2016/03/27/magazine/should-parents-of-severely-disabled-children-be-allowed-to-stop-their-growth.html?_r=0, accessed 19 November 2016.

²³² Allison J Pollock, Norman Fost and David B Allen, ‘Growth Attenuation Therapy: Practice and Perspectives of Paediatric Endocrinologists’ (2015) 100 Archives of disease in childhood 1185.

²³³ Douglas J Opel and Benjamin S Wilfond, ‘Cosmetic Surgery in Children with Cognitive Disabilities: Who Benefits? Who Decides?’ (2009) 39 The Hastings Center Report 19.

²³⁴ Renee D Boss and others, ‘Trisomy 18 and Complex Congenital Heart Disease: Seeking the Threshold Benefit’ (2013) 132 Pediatrics 161.

²³⁵ Anna Cereda and John C Carey, ‘The Trisomy 18 Syndrome’ (2012) 7 Orphanet journal of rare diseases 1.

²³⁶ Katherine E Nelson and others, ‘Survival and Surgical Interventions for Children with Trisomy 13 and 18’ (2016) 316 JAMA 420.

these youth does not work and the health risks are grave, even though clinical trials typically compare results from surgery to other weight-loss programs of unknown intensity and limited duration.²³⁷ Though the surgeries have shown short-term gains for reversal of diabetes and improvements to cardiac health, the most serious adverse events from these surgeries include the need to remove other organs (such as the gall bladder), kidney problems, the loss of bone density, the need for repeat surgeries, and severe psychological trauma for the minors, both from excess skin and the loss of high expectations after surgery.²³⁸ Clinicians are increasingly questioning whether the interventions are justified relative to non-medical options or whether they have properly been tested against those options, with even the most ardent advocates conceding that long-term outcomes of clinical trials are needed to properly define indications for and limitations of surgery.²³⁹

Different problems plague health care for critically ill children diagnosed with life-threatening or debilitating conditions. The care for many of these children overlaps considerably with clinical research because cures do not exist, while research on effective treatment is lacking. As a result, clinicians are compelled to do research and often encourage parents to submit their children to it. Even in the research context, however, regulations requiring a risk-benefit balance remain controversial, as direct benefits to a child undergoing research should be likely to outweigh risks that are not minimal or relatively minor in comparison before proceeding. Significant doubt continues to be cast as to whether children subjected to risk in clinical research are being used for tests for safety rather than for effective treatment – concerns that extend to practice overlapping such research.²⁴⁰ Critical questions remain, therefore, as to how these treatments relate to practice and whether parents and children are capable of understanding the relative uncertainties of risks and benefits, or the distinctions between research and standard care.

- ❖ In the field of *pediatric oncology*, considerable scientific uncertainty surrounds new and standard treatments. The lack of clear boundaries between clinical trials and clinical practice can raise significant concern as to whether the children are subjected to increased, unnecessary risk.²⁴¹ Recent data from some jurisdictions indicates that such children are enrolled in clinical trials at extremely high rates, with studies often showing that the children do not fully understand that they are involved in research.²⁴² Parents primarily enroll their children in these trials out of hope for cures, whereas clinicians enrolling the children often fail to warn of uncertainties or dispel parents' unrealistic hopes.²⁴³ Even in standard care, clinical use of statistical chances of survival for patients on the basis of past data is the norm. As a basic matter of prediction, these claims are fraught with scientific error, as even complete data of past outcomes cannot

²³⁷ Gunnar Göthberg and others, 'Laparoscopic Roux-En-Y Gastric Bypass in Adolescents with Morbid obesity—Surgical Aspects and Clinical Outcome' (2014) 23 *Seminars in Pediatric Surgery* 11. T Olbers and others, 'Two-Year Outcome of Laparoscopic Roux-En-Y Gastric Bypass in Adolescents with Severe Obesity: Results from a Swedish Nationwide Study (AMOS)' (2012) 36 *International journal of obesity* 1388.

²³⁸ Nianzhou Xiao and others, 'Kidney Function in Severely Obese Adolescents Undergoing Bariatric Surgery' (2014) 22 *Obesity* 2319. Anne-Marie D Kaulfers and others, 'Bone Loss in Adolescents after Bariatric Surgery' (2011) 127 *Pediatrics* e956.

²³⁹ AJ Beamish, SE Johansson and T Olbers, 'Bariatric Surgery in Adolescents: What Do We Know so Far?' (2014) *Scandinavian Journal of Surgery* 24. Kajsa Järholm and others, 'Two-Year Trends in Psychological Outcomes after Gastric Bypass in Adolescents with Severe Obesity' (2015) 23 *Obesity* 1966.

²⁴⁰ Wade (n 9). Lainie Friedman Ross, *Children in Medical Research: Access Versus Protection* (OUP Oxford 2006) 104–12.

²⁴¹ Jean-Claude K Dupont, Kathy Pritchard-Jones and François Doz, 'Ethical Issues of Clinical Trials in Paediatric Oncology from 2003 to 2013: A Systematic Review' (2016) 17 *The Lancet Oncology* e187. Christian M Capitini and others, 'Immunotherapy in Pediatric Malignancies: Current Status and Future Perspectives' (2014) 10 *Future Oncology* 1659.

²⁴² Aviva L Katz and others, 'Informed Consent in Decision-Making in Pediatric Practice' (2016) 138 *Pediatrics* e20161485.

²⁴³ For a survey of international studies, see Field and Behrman (n 14) 61. For recent studies showing strong indications that clinicians still fail to disclose uncertainty and counter parents' unrealistic hope, see Victoria A Miller and others, 'Hope and Persuasion by Physicians during Informed Consent' [2014] *Journal of Clinical Oncology* JCO. Tal Schechter and Ronald Grant, 'The Complexity of Consenting to Clinical Research in Phase I Pediatric Cancer Studies' (2015) 17 *Pediatric Drugs* 77.

predict the likelihood of future outcomes for individual patients.²⁴⁴ In cases of brain tumors, for example, five-year survival rates are often numerically calculated for children while acknowledging that data is limited to account for the location of the tumor, age, and other morbidities.²⁴⁵ Decisions to refrain from radiation therapy and to use chemotherapy and surgery alone are not recommended, even though long-term data on brain functioning, especially in young children, shows that children suffer tumor recurrence, seizures, and other mental health side effects after radiation therapy that are difficult to predict, raising questions of benefit to quality of life.²⁴⁶ Immunotherapy shows unusual promise in increasingly long-term survival in many cancers, even though outcomes from even early studies are poorly understood and may not be replicable,²⁴⁷ particularly in the case of pediatric brain cancers or tumors.²⁴⁸ Parents of children with these conditions, therefore, are likely to face considerable difficulty in anticipating how well treatment will benefit their children.

- ❖ *Pompe disease* and *Fabry disease* are rare genetic disorders marked by a failure to produce certain enzymes.²⁴⁹ Fabry disease results from the failure to produce an enzyme that permits glycolipids to accumulate in the organs and blood vessels, causing pain, vision impairment, dermatological symptoms and cardiac and kidney impairments. Children with Pompe disease lack the enzyme alpha-glucosidase, which metabolizes the complex carbohydrate glycogen into glucose. Without it, the glycogen accumulates at the cellular level, resulting in muscular-skeletal impairments, ranging from weakness to inability to eat or walk and in severe cases respiratory and cardiac failure. Early-onset symptoms can be life-threatening whereas late-onset symptoms may go undiagnosed for years. The European Medical Products Agency (EMPA) has approved regular enzyme-replacement therapy based on recombinant DNA technology for both conditions, lowering the threshold for testing because of their rare disease status and exceptional limitations on the ability to obtain quality data on how children fare with treatment.²⁵⁰ Despite the small numbers of patients and methodological shortcomings in the studies, the EMPA approved the drugs on the basis that the benefits appear to outweigh the risks, even though adverse effects may already be surfacing. In the case of Pompe disease, the EMPA has approved similar drugs on the condition that the

²⁴⁴ Douglas G Altman, 'Statistics and Ethics In Medical Research-Misuse Of Statistics Is Unethical' (1980) 281 *The British Medical Journal* 1182. Douglas G Altman, 'Statistics and Ethics in Medical Research. VII--Interpreting Results.' (1980) 281 *British Medical Journal* 1612.

²⁴⁵ Jennifer A Limond and others, 'Quality of Survival Assessment in European Childhood Brain Tumour Trials, for Children Aged 5 Years and over' (2015) 19 *European Journal of Paediatric Neurology* 202.

²⁴⁶ Nicole J Ullrich and others, 'Incidence, Risk Factors, and Longitudinal Outcome of Seizures in Long-Term Survivors of Pediatric Brain Tumors' (2015) 56 *Epilepsia* 1599. Kristen E Robinson and others, 'Predictors of Adaptive Functioning and Psychosocial Adjustment in Children with Pediatric Brain Tumor: A Report from the Brain Radiation Investigative Study Consortium' (2015) 62 *Pediatric blood & cancer* 509. Sumedh Subodh Shah and others, 'Long-Term Psychiatric Outcomes in Pediatric Brain Tumor Survivors' (2015) 31 *Child's Nervous System* 653. Karen A Kuhlthau and others, 'Prospective Study of Health-Related Quality of Life for Children With Brain Tumors Treated With Proton Radiotherapy' (2012) 30 *Journal of Clinical Oncology* 2079.

²⁴⁷ Capitini and others (n 241). Meenakshi Hegde and others, 'Cellular Immunotherapy for Pediatric Solid Tumors' (2015) 17 *Cytotherapy* 3.

²⁴⁸ Audrey Nailor and others, 'Highlights of Children with Cancer UK's Workshop on Drug Delivery in Paediatric Brain Tumours' (2016) 10 *ecancermedicallscience*. Eric K Ring and others, 'Checkpoint Proteins in Pediatric Brain and Extracranial Solid Tumors: Opportunities for Immunotherapy' [2016] *Clinical Cancer Research* clincanres.1829.2016.

²⁴⁹ Kliegman and others (n 14) 488–489, 499–500.

²⁵⁰ Fabrazyme. European Medicines Agency,

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000370/human_med_000784.jsp&mid=W00b01ac058001d124, accessed 19 November 2016. Replagal. European Medicines Agency, http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000369/human_med_001029.jsp&mid=W00b01ac058001d124, accessed 19 November 2016.

corporate manufacturer will continue outcome studies.²⁵¹ Long-term data on the safety of these drugs do not exist.

- ❖ *Epidermolysis bullosa* is a condition causing blistering of the skin and mucosal membranes, with varying degrees of the harm to the children. In its “simplex” form, the skin blisters from rubbing it and special care and topical treatments are required to spare the children injury. In its dystrophic form (DEB), the skin can separate by rubbing. Wounds may be difficult to heal, and, in some cases, esophageal blistering necessitates the use of nutritional tubes, whereas in severe cases chronic inflammation leads to carcinoma and death. In cases with severe junctional epidermolysis bullosa (JEB), the wound healing, infections, respiratory complications, and loss of proteins are so severe that most of these children do not survive past the first years of life. These children have been subjected to many experiments, such as bone marrow and stem cell therapies as well as subcutaneous injections to reduce blisters and lesions, only the latter of which have shown clear benefits meriting research and further testing.²⁵² Transplants have been performed on children with JEB as well as those with DEB, even though the science of the effect of such treatment on collagen repair is limited.²⁵³ Though some skin stability has occurred in JEB patients, both JEB and DEB children undergoing experimental stem cell therapy have not only been subjected to invasive procedures and skin grafts – some have died during the treatments. In the case, of JEB, the researchers of one recent study described the treatment as a “last-ditch attempt still lacking proof of efficacy” with “[s]ufficient initial thriving” as a goal.²⁵⁴

6.2.2 Analysis

In health care generally, clinicians acting in the best interests of the patients are expected to minimize harms to their patients and to provide treatment *only* when the benefits to each patient are expected to exceed risks. The most significant exception to that rule occurs in the area of research, where treatment may be tested on children that does not hold out the prospect of direct benefit *if* the treatment imposes minimal risk and minimal burden – or, in some jurisdictions, if special permission is given in extreme cases to justify the importance of subjecting children to potential discomfort and side-effects. The Explanatory Report to the Convention on Biomedicine, for example, elaborates that the proposed treatment undergoing research must be “likely to significantly improve” the child’s condition for research to go forward without meeting the more stringent test. Outside the context of research, however, the Convention defaults to professional standards, which are expected to be assessed for quality and adjusted to scientific advances, but without restrictions on clinical judgment to assure benefits and minimize risks to children. The Declaration of Helsinki permits unproven treatments to be used on patients to save lives, reestablish health or alleviate suffering – but without elaboration on these terms or how probable the benefits must be. The Declaration, in fact, permits an individual physician to use such therapy on the mere condition that the physician first seeks expert advice. Depending on the degree of discretion professional standards allow in the national legal orders, clinical judgment may permit a wide array of experimental and unproven treatments to be used in clinical

²⁵¹ Myozyme. European Medicines Agency, http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000636/human_med_000917.jsp&mid=W00b01ac058001d124, accessed 19 November 2016.

²⁵² Hiroshi Koga and others, ‘PDE4 Inhibition as Potential Treatment of Epidermolysis Bullosa Acquisita’ (2016) 136 *Journal of Investigative Dermatology* 2211.

²⁵³ Johanna Hammersen and others, ‘Genotype, Clinical Course, and Therapeutic Decision Making in 76 Infants with Severe Generalized Junctional Epidermolysis Bullosa’ (2016) 136 *Journal of Investigative Dermatology* 2150. Jo-David Fine, Becky Manes and Haydar Frangoul, ‘Systemic Granulocyte Colony-Stimulating Factor (G-CSF) Enhances Wound Healing in Dystrophic Epidermolysis Bullosa (DEB): Results of a Pilot Trial’ (2015) 73 *Journal of the American Academy of Dermatology* 56.

²⁵⁴ Hammersen and others (n 253). Fine, Manes and Frangoul (n 253).

practice, raising questions as to whether these treatments promote the *right to the highest attainable standard of health* for children.

For children with disabling conditions, the utilization of treatments without documented direct benefit clearly implicate *the right to physical and psychological integrity of the children*. Parents who stunt the growth of their children may, in fact, be in the best position to care for children but unable to do so if the children grow, much as parents of obese children may not have found ways to reduce that obesity, to the point that an individual child's health is at risk. Both of these examples, however, raise questions as to whether "health care" decisions are being made because of the lack of other support for the children, which otherwise might alleviate the need for invasive treatment. The same can be said of reconstructive surgeries on children with limited life spans who are subject to a wide array of interventions for physical anomalies. Withholding such treatment from the affected children may seem harmful or cruel, if the treatment would be provided to children who would live longer and might express their desire for the treatment, despite having to undergo other serious interventions for their physical health. The treatments may also be believed to improve the attachment of the parents to the child. When these treatments are made solely on the basis of the judgment and beliefs of clinicians and parents, the interests of the children may be marginalized – especially in cases where the child is young or disabled and unable to exercise *the right to consent* or *the right to be heard*.

For children with chronic life-threatening and debilitating conditions, treatments lacking in scientific support for their safety and efficacy may be as rare as the conditions they address or effective in some respects but with significant side effects. As a result, for the sake of the best possible outcomes, many children and their parents might believe experimental or unproven care is essential, given that "standard care" often fails or comes with considerable risks and side effects – or because no standard care exists at all. When considering governmental obligations to protect children from harm, however, more difficult questions arise, at a minimum, as to what assistance should be given to clinicians, parents, and especially children. Systemic governmental review of the scientific evidence to monitor the risks and benefits of treatment would seem essential, rather than deferring to producers of medication or leaving clinicians in individual cases or professional societies to do so. So, too, governments could, perhaps, be required to take action to ensure that parents and children are given accurate risk assessments so that the *right to informed consent* is not undermined, as well as the *right of a child to be heard*.

6.3 Children diagnosed with psychiatric disorders or severe mental health needs

6.3.1 Scientific background

Recently, both the Council of Europe and the EU Fundamental Rights Agency have taken initiatives to protect the rights of individuals injured in mental health practices. It is unclear, however, whether children are included in their proposed reforms.²⁵⁵ Nor do they appear to directly address the considerable scientific uncertainties in clinical psychiatry and psychology that may be behind inappropriate treatment, including for vulnerable persons unable to consent.

²⁵⁵ The Council of Europe is considering an additional protocol to the Convention on Biomedicine, though no protections for minors have been announced. Psychiatry. Council of Europe, <http://www.coe.int/en/web/bioethics/psychiatry>, accessed 19 November 2016. The EU has issued rights-based recommendations for protections of adults subjected to involuntary health measures. Involuntary placement and involuntary treatment of persons with mental health problems. Fundamental Rights Agency, http://fra.europa.eu/sites/default/files/involuntary-placement-and-involuntary-treatment-of-persons-with-mental-health-problems_en.pdf, accessed 19 November 2016.

While noninvasive treatment and counseling provide critical support for many individuals, including children, the risks associated with pharmacological treatment and involuntary restraints or invasive treatments on individuals are considerable, many resting on questionable scientific evidence. Because children as a class can be presumed not to consent to such treatment, invasive measures and their potential life-long effects should raise considerable concerns for human rights authorities. This is particularly so in Europe, where broad initiatives are now underway to reach large segments of the population, including children, with expanded mental health services, but without transparent scientific data substantiating their justifications for them.²⁵⁶

The scientific implications of current diagnoses and treatments in mental health care of children can be illustrated in several areas: (1) pharmacological treatments for children, both increasing in number and at young ages for behavioral and learning difficulties, (2) hospitalization of children without their consent, and (3) the current advances in the field toward focus on neuroscience and biological sciences to remedy gaps in evidentiary bases for mental health interventions. This last development raises particular concern as the field of child and adolescent psychiatry has been characterized by an increase in questionable diagnoses as well as an increase in pharmacological treatment of children, despite a lack of quality evidence about the risks and benefits.²⁵⁷ The current biomedical shift to research in neuroscience and genetics may leave many of these treatments inadequately researched or tested for their safety and efficacy.

Pharmacological Interventions

The use of pharmacology to abate mental stress and behavioral problems has generated significant critique, even for the most common, minor “disorders” diagnosed for children. *Attention Deficit Hyperactivity Disorder* (ADHD) is a diagnosis of inattention, overactivity, and impulsivity in children – traits that even proponents of the diagnosis indicate may be present in most children.²⁵⁸ The diagnosis, originating in 1902, has been contested for decades,²⁵⁹ without consistent criteria to distinguish it from other contested disorders, and with treatment outcomes assessed primarily via adults’ observations of children’s behavior. Recent research indicates that “ADHD” actually may manifest from attempts to start children too early in school,²⁶⁰ or that lack of physical activity may be connected with “need” for medications.²⁶¹ The leading US-based systemic review of evidence has indicated that standard medication can only be used for short

²⁵⁶ These claims suggest that more than one-fifth of all persons have mental health needs to be met with some kind of clinical support. WHO, *The European Mental Health Action Plan 2013-29* (2015) ii, 13. EU Joint Action on Mental Health and Wellbeing, *European Framework for Action on Mental Health and Wellbeing: Final Conference Report* (2016) 4.

²⁵⁷ Violeta V Stoyanova-Beninska and others, ‘The EU Paediatric Regulation: Effects on Paediatric Psychopharmacology in Europe’ (2011) 21 *European Neuropsychopharmacology: The Journal of the European College of Neuropsychopharmacology* 565. Celso Arango, ‘Child and Adolescent Neuropsychopharmacology: Now or Never’ (2011) 21 *European Neuropsychopharmacology* 563.

²⁵⁸ Mark J Scituito and Miriam Eisenberg, ‘Evaluating the Evidence For and Against the Overdiagnosis of ADHD’ (2007) 11 *Journal of Attention Disorders* 106.

²⁵⁹ Sami Timimi, ‘A Critique of the International Consensus Statement on ADHD’ (2004) 7 *Clinical child and family psychology review* 59.

²⁶⁰ Linda Halldner and others, ‘Relative Immaturity and ADHD: Findings from Nationwide Registers, Parent- and Self-Reports’ (2014) 55 *Journal of Child Psychology and Psychiatry, and Allied Disciplines* 897. Chen M and others, Mu-Hong Chen and others, ‘Influence of Relative Age on Diagnosis and Treatment of Attention-Deficit Hyperactivity Disorder in Taiwanese Children’ (2016) 172 *The Journal of Pediatrics* 162. Richard L Morrow and others, ‘Influence of Relative Age on Diagnosis and Treatment of Attention-Deficit/hyperactivity Disorder in Children’ (2012) 184 *CMAJ: Canadian Medical Association Journal* 755.

²⁶¹ Ole Jakob Storebø and others, ‘Methylphenidate for Children and Adolescents with Attention Deficit Hyperactivity Disorder (ADHD)’ [2015] *The Cochrane Database of Systematic Reviews* CD009885. Salima Punja and others, ‘Amphetamines for Attention Deficit Hyperactivity Disorder (ADHD) in Children and Adolescents’, *Cochrane Database of Systematic Reviews* (John Wiley & Sons, Ltd 2016). Edmund JS Sonuga-Barke, ‘Can Medication Effects Be Determined Using National Registry Data? A Cautionary Reflection on Risk of Bias in “Big Data” Analytics’ (2016) 80 *Biological Psychiatry* 893. Xinyue Liu and others, ‘Psychotropic Drug Utilization in Children with Concurrent Attention-Deficit/hyperactivity Disorder and Anxiety’ (2014) 28 *Journal of Anxiety Disorders* 530.

periods of time, but even then yields at least a “few” adverse events; under standard usage, children could be expected to experience headaches, nausea, and anxiety from medication.²⁶² Other researchers have raised concern about the lack of consent of children medicated against their will.²⁶³

Scientific shortcomings equally manifest at the opposite end of the spectrum of mental health disorders, including well-known diagnoses such as *schizophrenia*. The diagnosis formally dates back to 1908, marked by an oft-neglected awareness that its defining characteristics are poorly understood and may be a bundle of related conditions.²⁶⁴ Indeed, the architects of the current DSM have conceded that the recently revised criteria for diagnosing schizophrenia have many “shortcomings” that are “easy to numerate” and that it is “difficult” to come up with valid criteria.²⁶⁵ Systematic reviews of evidence indicate high rates of false diagnosis in triage, whereas even standard diagnostic measures may result in misdiagnosis of individuals with schizophrenia.²⁶⁶ Nevertheless, under the most recent and often-cited guidelines for treatment of children and adolescents diagnosed with schizophrenia, antipsychotic medication is the primary treatment, even though there is limited evidence of its efficacy in young people, with concern that young children and adolescents may react adversely both physically and psychologically to those medications more than adults do.²⁶⁷ Psychological interventions and behavior therapy are considered less invasive but are not utilized because data on their efficacy is largely unavailable – in turn, because alternatives are not studied, which reinforces favor for pharmacology, despite its own evidentiary problems.²⁶⁸ In fact, recent long-term controlled studies of patients indicates that patients may be likely to fare better with as little medication as possible and multidisciplinary, family-oriented counseling than with traditional treatment.²⁶⁹

Across the spectrum of illnesses, the medical literature continues to report that pharmacological treatment is the treatment of choice for mental health matters despite serious scientific doubts. The diagnostic criteria for bipolar disorder (BPD), for example, have been considered sufficiently vague to be the cause in inexplicable surges of diagnoses of the disorder in the US and Europe.²⁷⁰ And yet, as of 2016, children continue to be subjected to antipsychotic drugs for BPD diagnoses and other psychoses and mood disorders, with uncertain risks and benefits ascribed to the medication.²⁷¹ New drugs, such as aripiprazole, are widely touted to have less effect on young

²⁶² Agency for Healthcare Research Quality, ‘Attention Deficit Hyperactivity Disorder: Effectiveness of Treatment in At-Risk Preschoolers; Long-Term Effectiveness in All Ages; and Variability in Prevalence, Diagnosis, and Treatment’ (2011) 44 Comparative Effectiveness Review.

²⁶³ Karen-Lis Kristensen and Line Lerche Mørck, ‘ADHD Medication and Social Self-Understanding’ (2016) 31 European Journal of Psychology of Education 43. Alice Charach and others, ‘Exploring Stimulant Treatment in ADHD: Narratives of Young Adolescents and Their Parents’ (2014) 14 BMC psychiatry 1.

²⁶⁴ Daisy Yuhas, ‘Evolution of Schizophrenia’ (2013) 24 Scientific American Mind 63.

²⁶⁵ Rajiv Tandon and others, ‘Definition and Description of Schizophrenia in the DSM-5’ (2013) 150 Schizophrenia research 3.

²⁶⁶ Hanna Bergman and others, ‘Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) for Diagnosing Schizophrenia in Children and Adolescents with Psychotic Symptoms’, *Cochrane Database of Systematic Reviews* (John Wiley & Sons, Ltd 2015).

²⁶⁷ National Institute for Health and Care Excellence (UK), Psychosis and schizophrenia in children and young people: recognition and management (2013 & 2016 update). NICE, <https://www.nice.org.uk/guidance/cg155>, accessed 19 November 2016.

²⁶⁸ *ibid.*

²⁶⁹ John M Kane and others, ‘Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program’ (2015) 173 American Journal of Psychiatry 362.

²⁷⁰ Carmen Moreno and others, ‘National Trends in the Outpatient Diagnosis and Treatment of Bipolar Disorder in Youth’ (2007) 64 Archives of general psychiatry 1032. Joseph C Blader and Gabrielle A Carlson, ‘Increased Rates of Bipolar Disorder Diagnoses among U.S. Child, Adolescent, and Adult Inpatients, 1996-2004’ (2007) 62 Biological psychiatry 107.

²⁷¹ Marie-Line Menard and others, ‘Incidence of Adverse Events in Antipsychotic-Naïve Children and Adolescents Treated with Antipsychotic Drugs: A French Multicentre Naturalistic Study Protocol (ETAPE)’ (2016) 6 BMJ Open e011020. René Ernst Nielsen and others, ‘Risk of Diabetes in Children and Adolescents Exposed to Antipsychotics: A Nationwide 12-Year Case-Control Study’ (2014) 53 Journal of the American Academy of Child and Adolescent Psychiatry 971. Britta Galling and others, ‘Type 2 Diabetes Mellitus in Youth Exposed to Antipsychotics: A Systematic Review and Meta-Analysis’ (2016) 73 JAMA

people diagnosed with schizophrenia, BPD, and mood disorders because it produces less physical risks, but patients also report insomnia, spasms, tremors, and suicidal thoughts.²⁷² Even for more mild mental health problems, such as depression, the use of antidepressants on minors generally lacks substantial scientific support.²⁷³ Systemic analysis has not been done to determine whether most mental health disorders affecting children could be better treated without pharmacology – particularly whether the actual health conditions of children are improved by it or whether it is instead simply an expedient way to manage a range of mental health and behavioral concerns.

Restraints on liberty through involuntary hospitalization and civil commitment

Throughout Europe, substantial documentation of rates of involuntary hospitalization and civil commitment of children, in general, is lacking. Research documenting the scientific validity of such treatment is also difficult to locate. This is not surprising, as the limited research on mental health services alone indicates wide differences in care that is difficult to ascribe to a theory that some regions of Europe experience higher rates of mental illness than others. In nations where study does occur, research casts doubt on the scientific foundations of clinical practices. In Germany, the training and standards have been called into question.²⁷⁴ Recent studies in Sweden have acknowledged that scientific bases for the commitment of young people are dubious and inconsistent.²⁷⁵ In Finland, where involuntary hospitalization has been unusually high, the bias in favor of hospitalization among mental health professionals has been documented by Finnish researchers, where recent reductions and other changes in hospitalization over time have fluctuated so much, without explanatory data, that researchers are uncertain whether practice changes are responsible for the outcomes or mental health disorders have declined.²⁷⁶

The absence of data confirming the benefits and necessity of these treatments in Europe itself should raise considerable alarm, as both the Council of Europe and the EU Agency for Fundamental Rights have raised concerns about the violations of the rights of adults from mental health practices. Extending this concern to children is appropriate because involuntary hospitalization and civil commitment result not only on restraints in liberty but may be accompanied by involuntary medication and electroshock therapy.²⁷⁷ Children with intellectual

psychiatry 247. Ajit Kumar and others, 'Atypical Antipsychotics for Psychosis in Adolescents' [2013] The Cochrane Database of Systematic Reviews CD009582.

²⁷² Klaus Damgaard Jakobsen and others, 'Neurological, Metabolic, and Psychiatric Adverse Events in Children and Adolescents Treated With Aripiprazole' (2016) 36 *Journal of Clinical Psychopharmacology* 496. Tamison Doey, 'Aripiprazole in Pediatric Psychosis and Bipolar Disorder: A Clinical Review' (2012) 138, Supplement *Journal of Affective Disorders* S15. Aripiprazole for autism spectrum disorders (ASD). Cochrane, http://www.cochrane.org/CD009043/BEHAV_aripiprazole-autism-spectrum-disorders-asd, accessed 19 November 2016. Priya Khanna and others, 'Aripiprazole versus Other Atypical Antipsychotics for Schizophrenia' [2013] The Cochrane Database of Systematic Reviews CD006569.

²⁷³ Georgina R Cox and others, 'Psychological Therapies versus Antidepressant Medication, Alone and in Combination for Depression in Children and Adolescents' [2012] The Cochrane Library.

²⁷⁴ Thomas Lempp, Monika Heinzl-Gutenbrunner and Christian Bachmann, 'Child and Adolescent Psychiatry: Which Knowledge and Skills Do Primary Care Physicians Need to Have? A Survey in General Practitioners and Paediatricians' (2016) 25 *European Child & Adolescent Psychiatry* 443. Thomas W Kallert, Matthias Glöckner and Matthias Schützwohl, 'Involuntary vs. Voluntary Hospital Admission' (2008) 258 *European Archives of Psychiatry and Clinical Neuroscience* 195. Jasmin Jendreyshak and others, 'Voluntary versus Involuntary Hospital Admission in Child and Adolescent Psychiatry: A German Sample' (2014) 23 *European Child & Adolescent Psychiatry* 151.

²⁷⁵ Veikko Peltö-Piri and others, 'Justifications for Coercive Care in Child and Adolescent Psychiatry, a Content Analysis of Medical Documentation in Sweden' (2016) 16 *BMC health services research* 66. For a recent government report, see SOU 2015:71, *Barns och ungas rätt vid tvångsvård. Förslag till ny LVU, Del A*, 315-317, 411.

²⁷⁶ Suvi Turunen, Maritta Välimäki and Riittakerttu Kaltiala-Heino, 'Psychiatrists' Views of Compulsory Psychiatric Care of Minors' (2010) 33 *International Journal of Law and Psychiatry* 35. Heikki Toivo Ellilä and others, 'The Involuntary Treatment of Adolescent Psychiatric inpatients—A Nation-Wide Survey from Finland' (2008) 31 *Journal of Adolescence* 407. Kim Kronström and others, 'Changes in the Clinical Features of Child and Adolescent Psychiatric Inpatients: A Nationwide Time-Trend Study from Finland' (2016) 70 *Nordic Journal of Psychiatry* 436.

²⁷⁷ Pia Nordanskog and others, 'Electroconvulsive Therapy in Sweden 2013: Data From the National Quality Register for ECT' (2015) 31 *The Journal of ECT* 263. Arlette Scheifes and others, 'Prevalence and Characteristics of Psychotropic Drug Use in Institutionalized Children and Adolescents with Mild Intellectual Disability' (2013) 34 *Research in Developmental Disabilities*

disabilities may also be disproportionately impacted by these measures.²⁷⁸ Given the history of questionable hospitalization and abusive practices associated with it, the lack of commitment from human rights authorities and European legal orders to investigate the security of children in mental health services makes it difficult to determine whether that security exists.

Neurological science and the impact on quality of scientific evidence

In the last decade, many of the benefits of psychiatry and psychology have been dismissed under the weight of several scientific critiques – not only from the study of clinical practice in general but broad and detailed biomedical challenges to the scientific nature of both disciplines.²⁷⁹ One of the first turning points came from a series of discoveries in genetics and neuroscience that challenged many of the claims that psychiatric disorders could be diagnosed with distinction.²⁸⁰ These discoveries have fueled criticisms of the inherent subjectivity of mental health professions in diagnosing and treating conditions as disorders. Indeed, despite constant revisions of mental health manuals such as the DSM and ICD to remove notoriously unsound diagnoses, the current DSM has expanded its pathologies to cover certain manifestations of grief, binge eating, and forgetfulness due to old age, diagnoses that have been greeted with considerable ridicule.²⁸¹ Most recently, psychology has come under equal criticism by researchers who have attempted to replicate studies performed and found that most could not be replicated.²⁸² All of these concerns have reinforced suspicions that the use of psychiatry and psychology to justify invasive treatments is problematic.²⁸³

Unfortunately, these criticisms have only culminated in a loss of acknowledgment of the value of noninvasive mental health care, accompanied by a sharp debate over whether traditional psychiatry should ground its work more in biomedicine and neuroscience to develop diagnoses and treatment interventions.²⁸⁴ The US National Institute of Mental Health, for example, has deprioritized psychiatry research without a biological component.²⁸⁵ The downside of this scientific development is that the dominant practices in child and adolescent psychiatry that already lack support may continue without the scientific data to determine the safety and efficacy of their continued use on children. Research on these therapies to date has provided the very evidence that has questioned ongoing practices; lack of research could further obscure their usage on children.

3159. J Aa Nøttestad and OM Linaker, 'Psychotropic Drug Use among People with Intellectual Disability before and after Deinstitutionalization' (2003) 47 *Journal of intellectual disability research: JIDR* 464.

²⁷⁸ Björn Ramel and others, 'Overrepresentation of Unaccompanied Refugee Minors in Inpatient Psychiatric Care' (2015) 4 *SpringerPlus* 131. Arlette Scheifes and others, 'Adverse Events and the Relation with Quality of Life in Adults with Intellectual Disability and Challenging Behaviour Using Psychotropic Drugs' (2016) 49-50 *Research in Developmental Disabilities* 13.

²⁷⁹ Allen J Frances and John M Nardo, 'ICD-11 Should Not Repeat the Mistakes Made by DSM-5' (2013) 203 *The British Journal of Psychiatry* 1.

²⁸⁰ This work began with construction of genetic databases, see Chapter 4.1, which led to a series of discoveries in this regard. Hreinn Stefansson and others, 'Common Variants Conferring Risk of Schizophrenia' (2009) 460 *Nature* 744. Jianxin Shi and others, 'Common Variants on Chromosome 6p22.1 Are Associated with Schizophrenia' (2009) 460 *Nature* 753. See Stephan Ripke and others, 'Biological Insights from 108 Schizophrenia-Associated Genetic Loci' (2014) 511 *Nature* 421.

²⁸¹ Frances and Nardo (n 279).

²⁸² In the field of psychology, the debate has heightened after a large scale multidisciplinary project retesting 100 studies in psychology published in 2015 was only able to reproduce statistically similar results in one third of those studies. See Open Science Collaboration, 'Estimating the Reproducibility of Psychological Science' (2015) 349 *Science* 943.

²⁸³ Tomasz Witkowski, *Psychology Gone Wrong: The Dark Sides of Science and Therapy* (Universal-Publishers 2015); Scott O Lilienfeld, Steven Jay Lynn and Jeffrey M Lohr, *Science and Pseudoscience in Clinical Psychology, Second Edition* (Guilford Publications 2014).

²⁸⁴ See S Kapur, AG Phillips and TR Insel, 'Why Has It Taken so Long for Biological Psychiatry to Develop Clinical Tests and What to Do about It?' (2012) 17 *Molecular Psychiatry* 1174. Nick Craddock and Michael J Owen, 'The Kraepelinian Dichotomy - Going, Going... but Still Not Gone' (2010) 196 *The British Journal of Psychiatry: The Journal of Mental Science* 92. Sandra J Tanenbaum, 'Evidence-Based Practice as Mental Health Policy: Three Controversies and a Caveat' (2005) 24 *Health Affairs (Project Hope)* 163.

²⁸⁵ Sara Reardon and others, 'NIH Rethinks Psychiatry Trials' (2014) 507 *Nature* 288.

6.3.2 Analysis

Physical interventions on children in the pursuit of their mental health have a long history of resting on speculative evidence and theory. The systematic reviews of evidence to date indicate that medication may mute negative behavioral or emotional symptoms but that their side effects on children are unknown, particularly regarding their effects on the brain, which they target by design. The *right to the highest attainable standard of health* and *right to physical and psychological integrity* are threatened by these interventions, particularly if noninvasive treatments would provide better alternatives to the child. For children subjected to involuntary commitment and hospitalization, *the right to personal liberty* is clearly compromised, with potential for treatment that may be considered *degrading* and *inhumane*. In all of these cases, the degree to which force occurs is under-researched, with risks to *the right of the child to be heard* and *the right to consent*. Research on the quality of care is only the first step to fulfilling positive obligations of governments to protect the children concerned.

6.4 Summary of the rights at stake

The variety of biomedical interventions that are deployed for children diagnosed with serious health needs corresponds in part to the diversity of physical impairments for children with rare diseases and chronic illnesses. They are also amplified by physical interventions that are used for the mental health benefits of children, both for children diagnosed with minor mental impairments and those with severe physical and mental health problems. The invasiveness of these treatments, whether likely to benefit the children or not, poses considerable risks to numerous rights of children associated with their physical and psychological integrity, their right to autonomy and be heard, in addition to their right to the highest attainable standard of health. Taken together, they raise numerous questions as to whether these interventions should be entrusted to clinical judgment and professional standards, rather than to thorough and continuous review for high quality, scientifically sound care.

Scientific challenge/procedure	Rights at stake
Interventions on children with chronic physical illnesses	<ul style="list-style-type: none">• Right to the highest attainable standard of health• Right to physical and psychological integrity• Right to participate in decisions affecting the child• Right to informed consent
Interventions on the body for mental health conditions	<ul style="list-style-type: none">• Right to the highest attainable standard of health• Right to physical and psychological integrity• Right to personal liberty



7. Transplantation

7.1 Introduction

The transplantation of organs, tissues, and cells constitutes one of the most complex categories of biomedical interventions, in no small part because different transplantations, grouped conceptually, vary significantly in the ways that they are implemented and regulated. Organ transplantation requires donation from another person (*allogeneic transplantation*). Though this form of transplantation is often the treatment of choice for most conditions, cell transplantation for some conditions often can involve removal of a patient's cells to be treated and transplanted back into the body (*autologous transplantation*).²⁸⁶ From a medico-legal perspective, problems with organ supply and harvesting have led to extensive regulation of organ donations, but donations of tissues and cells, which naturally regenerate, have not been subject to similar regulatory controls. When children are involved, these matters become more complicated. Most European jurisdictions appear to legally restrict children from being living organ donors in some way, which means that many children are often dependent on organs from others who have died – especially other children – and are often on the same waiting lists with adults, in the absence of directed donation from an adult. In contrast, thousands of children each year receive tissue and cell transplants from other children because such transplantations provide both the best matches for the recipients and presumptively relatively lesser risks for donor children. This is especially true for hematopoietic stem cell transplantation (HSCT), which is often recommended to treat various forms of pediatric leukemia, anemia, and immune disorders, but is now being used as experimental care on other rare conditions, often without the benefit of long-term clinical trials.

This chapter addresses the rights of children as recipients and donors for transplantations. As a whole, the chapter reflects a unique field in biomedicine in which the ability of some children to receive the highest attainable standard of health care may depend on risks taken with the physical and psychological integrity of other children. And yet, while transplantation is essential for many pediatric patients' survival, their right to the highest attainable standard of health may also be undermined by scientific uncertainties regarding projected outcomes from transplantation and the transplantation process in general. This chapter, therefore, begins with an overview of the variable scientific advances and uncertainties in transplantations and their potential impact on recipients, including experimental transplantations in clinical practice. It then examines those advances and uncertainties that apply to children as donors, namely (1) those regarding death determinations of minors and (2) the risks to children as living donors, particularly where the donations occur within families.

7.2 Children as transplantation recipients

7.2.1 Scientific background

Transplantation itself is a high-risk medical intervention that is often justified by the severity of a patient's condition, such as end-stage organ failure or disease with high rates of mortality or

²⁸⁶ *Autologous* or *autogenic* transplantation refers to biological matter removed from the patient, treated or modified and transplanted back into the patient's body. *Allogeneic* transplantation refers to transplantation with organs or tissues of another, which can also be *syngeneic* if the donated organ or tissue comes from an identical twin.

morbidities.²⁸⁷ The actual transplantation, however, is only part of the treatment process. Immunotherapy and other medications to avoid rejection or fight complications are often required. For leukemia patients, chemotherapy precedes transplantation.²⁸⁸ The benefits and risks of any one type of transplantation also vary from child to child. In organ transplantation, for example, 1-year survival rates are high for children as a class but drop considerably over time: adolescents may face greater risks of graft loss and rejection relative to young children due to changes in the body, even though the risks and benefits of post-transplant medications may be more uncertain for younger recipients.²⁸⁹ With HSCT, survival rates are higher after the first remission but much lower after a second, and children of all such donations may suffer from debilitating infections or fatal graft-versus-host disease (GVHD), the latter from allogeneic donations, which are still “the treatment of choice” because the cells come from healthy children.

For all pediatric patients, the scientific risks and uncertainties may make it difficult for parents and patients themselves to compare treatment alternatives, not only for the transplantation itself but also for other associated treatments necessary to make them successful, only some of which are required to go through careful testing and clinical trials.²⁹⁰ Sound scientific methods for comparing these outcomes is lacking, and it remains unclear whether different forms of transplantation have been systematically studied to determine whether projected outcomes are warranted when applied to individual cases. More troublingly, perhaps, the successes of HSCT for some illnesses have led clinicians to experiment with their use for patients with rare conditions, but not always in clinical trials or where the likelihood of benefits is well established before they are tested on children. As seen in Chapter 6, this has been the case for children with epidermolysis bullosa, but it is also true for other conditions, such as multiple sclerosis, where transplantation is being touted commercially without quality data supporting it.²⁹¹ One of the most notorious biomedical controversies in Europe recently has involved the development of artificial trachea transplants seeded with stem cells; the practice was recently halted due not only to scientific and regulatory misconduct but because of presumptions that the treatment could be used on patients as exceptional care as other options were presumed unavailable.²⁹² Children died following these transplants, for reasons that have yet to be explained or clearly attributable to their conditions.²⁹³ In all of these cases, it remains very unclear whether systematic oversight of medico-legal systems is in place to determine whether treatment decisions are being made on the basis of quality evidence of the benefit of transplantations for children.

²⁸⁷ Except where noted, this section is drawn from Kliegman and others (n 14) 753–763.

²⁸⁸ Navneet S Majhaal and others, ‘Recommended Screening and Preventive Practices for Long-Term Survivors after Hematopoietic Cell Transplantation’ (2012) 5 *Hematology/oncology and stem cell therapy* 1.

²⁸⁹ Israel Henig and Tsila Zuckerman, ‘Hematopoietic Stem Cell Transplantation—50 Years of Evolution and Future Perspectives’ (2014) 5 *Rambam Maimonides Medical Journal* <<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4222417/>> accessed 18 November 2016. Daphne T Hsu, ‘Biological and Psychological Differences in the Child and Adolescent Transplant Recipient’ (2005) 9 *Pediatric transplantation* 416.

²⁹⁰ Amber O Molnar and others, ‘Generic Immunosuppression in Solid Organ Transplantation: Systematic Review and Meta-Analysis’ (2015) 350 *BMJ* h3163. See also European Medical Products Agency, *Guideline on Clinical Investigation of Immunosuppressants for Solid Organ Transplantation* (2008), Doc. Ref. CHMP/EWP/263148/06, 14.

²⁹¹ Risky stem cell treatment ‘halts progress of multiple sclerosis’. U.S. National Library of Medicine, <https://www.ncbi.nlm.nih.gov/pubmedhealth/behindtheheadlines/news/2016-06-10-risky-stem-cell-treatment-halts-progress-of-multiple-sclerosis/>, accessed 18 November 2016.

²⁹² For the initial defense that these therapies were permissible as exceptional use without regard to research, see Karolinska Institute, *Suspected scientific misconduct in the case of Paolo Macchiarini*, Dnr 2-2184/2014 (2015). For ongoing coverage, see Karolinska Institutet, <http://ki.se/en/news/macchiarini>, accessed 18 November 2016.

²⁹³ For instances involving child patients who were used to advance the science in clinical practice, see Gretchen Vogel, ‘Trachea Transplants Test the Limits’ (2013) 340 *Science* 266. Paolo Macchiarini: A surgeon’s downfall, BBC, <http://www.bbc.com/news/magazine-37311038>, accessed 18 November 2016. Girl Dies After Groundbreaking Trachea Transplant. ABC News, <http://abcnews.go.com/Health/girl-dies-groundbreaking-trachea-transplant/story?id=19604605>, accessed 18 November 2016.

7.2.2 Analysis

Both the right to *the highest attainable standard of health* and *the right to life* of children may be seen as implicated by transplantations, which are designed to prolong life or improve its quality. Collective data based on overall short-term outcomes purportedly favor the risk for recipients' survival in many of these cases, even when it is unclear if many of the patients would not have lived longer without the transplantation – perhaps with an impaired quality of life. The medical literature is replete with projected chances of survival of patients with many forms of transplantation, but the literature is not transparent as to the bases for these claims – for example, whether they are consistently updated on the basis of long-term data from national registries or drawn from a smaller set of studies and assumed to hold as predicted outcomes when extrapolated to all patients. For children who would prefer not to undergo transplantation, it is further unclear what protocols exist to determine whether the child has the *right to consent* to the treatment and *right to be heard*; as a matter of law, in many jurisdictions, parents and children may not refuse treatment perceived as life-saving. Children with leukemia, however, must often endure chemotherapy before the transplant, plus endure the transplant process and subsequent side effects and after-care. Children who have been through one round of transplantation may not wish to endure another. In cases where the likelihood of survival is decreased or uncertain, the children may prefer to live out the remainder of their lives without the agony of treatment. These matters raise fundamental questions as to whether deference to professional standards and parental consent is suitable for each child in each case, or whether transplantations for children should be systemically monitored with quality support to ensure, at a minimum, that patients and their parents fully understand the quality of the data used to justify treatment decisions.

7.3 Children as potential donors at death

7.3.1 Scientific background

For most children, laws governing donation after death require parents to consent to donation of organs and tissues if the child has not consented to donation before death. In opt-out donation jurisdictions, the same rule appears to apply, even though the failure to opt-out appears to attach automatically at age 18, leaving it unclear whether such an individual is expected to consider opting out as a child, as well as whether such a child is properly informed to understand that the automatic “opt-in” will attach as soon as legal childhood ends. For most children, however, their protection appears to depend on their parents, who in turn depend on determinations of death by clinicians, many of which are the subject of considerable ongoing scientific controversy.

Because advances in health care have reduced child mortality, the number of available pediatric donors has also been reduced.²⁹⁴ Pediatric donor organs have also been increasingly used on adult donors, raising additional questions as to whether children who need donations from other children have sufficient access to donor organs.²⁹⁵ Donation after brain death (DBD) is believed to reduce opportunities for donations, with an impact on potential recipients, including young children and infants. Brain death determinations in infants and neonates, in particular, are difficult, even more so because a child declared brain dead might be on life support, which must then be removed. Advocacy for donation after circulatory determination of death (DCDD) is,

²⁹⁴ JK Workman and others, 'Pediatric Organ Donation and Transplantation' (2013) 131 *Pediatrics* e1723. J Brierley and A Hasan, 'Aspects of Deceased Organ Donation in Paediatrics' (2012) 108 *British Journal of Anaesthesia* i92.

²⁹⁵ Brierley and Hasan (n 294). E Charles, A Scales and J Brierley, 'The Potential for Neonatal Organ Donation in a Children's Hospital' (2014) 99 *Archives of Disease in Childhood - Fetal and Neonatal Edition* F225. Ilias Chatziioannidis, Pagona Chouchou and Georgios Mitsiakos, 'Newborns as Potential Organ Donors: A New Perspective?' (2015) 4 *Journal of Pediatric and Neonatal Individualized Medicine (JPNIM)* e040114.

therefore, on the rise. Both DBD and DCDD in children can be questioned on scientific grounds. DCDD, however, raises questions about how donation is reconciled with the uncertainty of brain death.²⁹⁶ Moreover, advocacy for DCDD does not appear to rest on the basis of relatively less scientific uncertainty, but rather on its benefit for organ donation supply.²⁹⁷ This is particularly true in the field of neonatal care, where neonatal mortality has been significantly reduced and the pressure for neonatal donations is considerable, despite the fact that both brain death determinations and cardio-respiratory death determinations are difficult.²⁹⁸ No medical consensus appears to exist in favor of DCDD, though its usage is growing.

7.3.2 Analysis

Organ and tissue donation among children raises considerably difficult questions about ensuring *the right to the highest attainable standard of health* of critically ill children as a whole who need transplants, while also protecting children who face a high likelihood of death but who – while living or if they were to survive – are entitled to the same rights of other children. This matter becomes even more complex when examining *the right to life* for both groups of children. From a scientific point of view, a child whose death has been determined on the basis of its cardio-respiratory functions may have little chance of life from a neurological point of view, but the difficulty in measuring brain death and chance of circulatory recovery raise fundamental questions as to whether brain death determinations should be abandoned even in part because doing so might increase donor supply. Open advocacy for DCDD continues to gain favor but is not universally supported as scientifically sound.²⁹⁹ The European Society for Paediatric & Neonatal Intensive Care Society favors brain-death determinations before transplantation, with referral to donor organizations once such testing is underway.³⁰⁰ For countries that permit DCDD, however, those same guidelines only recommend that specialist teams should be involved before life support is withdrawn. These and other guidelines take no position on the family's right to make the final determination to draw life support in cases of brain death. Current discourse on the rights of the affected children is difficult to locate in the medical literature.

7.4 Children as living donors

7.4.1 Scientific background

Though it is unclear how often children may be living donors to adults or others outside of their own families, most evidence indicates that children are likely to be donors when their siblings need transplantation.³⁰¹ From a purely biomedical view, the need for sibling donors is not unique to children. The key difference, however, is that the consent of the donor in the case of children comes from a parent, who also may be presumed to request or consent to the donation for the recipient child, on the legal presumption that the best interests of both children will be served.

When children are critically ill requiring tissue and cell donation, the chances of survival, as explained above, are better if the tissues and cells are from a healthy donor. Existing siblings may

²⁹⁶ Dale Gardiner and Andrew McGee, 'Death, Permanence and Current Practice in Donation after Circulatory Death' [2016] QJM hew184.

²⁹⁷ Chatziioannidis, Chouchou and Mitsiakos (n 295). Charles, Scales and Brierley (n 295).

²⁹⁸ Ajit A Sarnaik, 'Neonatal and Pediatric Organ Donation: Ethical Perspectives and Implications for Policy' (2015) 3 *Frontiers in Pediatrics*.

²⁹⁹ Joseph A Carcillo and others, 'A Call for Full Public Disclosure and Moratorium on Donation after Cardiac Death in Children' (2010) 11 *Pediatric Critical Care Medicine* 641. Sarnaik (n 298).

³⁰⁰ ESPNIC Standards for End of Life Care. ESPNIC, <http://espnice-online.org/About/ESPNIC-Standards-for-End-of-Life-Care>, accessed 18 November 2016.

³⁰¹ Adolescents in some European jurisdictions may donate organs, but the regulation overall is restrictive. M Campbell and others, 'How Young Is Too Young to Be a Living Donor?' (2013) 13 *American Journal of Transplantation* 1643.

be considered as potential donors since they have a 25 % chance of being a match with the recipient.³⁰² In addition to this, a child may be conceived – either naturally or with the help of ART – for the purpose of providing biological material (primarily cord blood cells) for an older sibling with an inherited disease. Sibling donors have been used in an estimated 39-48 % of all childhood transplantations (blood and bone marrow), and an estimated 600–700 children in Europe are HSCT donors for their siblings every day.³⁰³

The risk calculation for the donor child is challenging as the only benefit to that child is emotional or psychological, whereas the transplantation procedures include both short and long-term physical and psychological risks.³⁰⁴ The physical risks to the child may be minimized but may still be significant. Harvesting procedures for bone marrow transplantation between siblings includes complications such as pain, anemia, cardiovascular disturbances, anesthesia complications, and prolonged hospital stays.³⁰⁵ Organ donation involves several perioperative risks, including the risk of death from infection.³⁰⁶ Indeed, the potential donor may suffer psychological trauma from guilt from objecting to transplantation after being asked to consent, but also from transplantation not being successful and a sense of failure.³⁰⁷ Depression, withdrawal, behavioral problems, lowered self-esteem, identity problems, psychopathology, guilt, resentment, and anger may also follow the donation procedure.³⁰⁸ When organ donation is possible, the child may also feel neglected, have lingering concerns about scarring, or harms to self-image being affected and self-esteem being lowered.³⁰⁹ Little discourse in the medical literature can be found on whether any large-scale study has been done on reducing these harms by finding ways to listen to the potential donor child and engaging the child in the decision.

7.4.2 Analysis

From a legal point of view, it may seem unsurprising that a child may donate cells and tissues, at a minimum, without being required to consent to it, given that only parental consent is required under most donation guidelines as is true for most medical interventions. It could be questioned, however, how far parental rights extend to invasive measures on children that are not for the benefit of those children. Beyond parental protection, the standards of protection in the national legal orders are unclear.³¹⁰ If parental consent alone governs the decisions, it is understandable that the parents' interest in saving one child may prevent the parents from being objective as to whether consent would be given for their child to be a donor for transplantation in other circumstances. Even granting a child the right to consent or object may not be sufficient protection where the child feels pressured to consent.

The use of children as living donors may also be scientifically and legally challenging for a variety of reasons, given the uncertainty of the cognitive development of the child to exercise *the right to*

³⁰² Lori S Wiener and others, 'Sibling Stem Cell Donor Experiences at a Single Institution' (2008) 17 *Psycho-oncology* 304.

³⁰³ Jan Styczynski and others, 'Risk of Complications during Hematopoietic Stem Cell Collection in Pediatric Sibling Donors: A Prospective European Group for Blood and Marrow Transplantation Pediatric Diseases Working Party Study' (2012) 119 *Blood* 2935.

³⁰⁴ Lainie Friedman Ross, J Richard Thistlethwaite and others, 'Minors as Living Solid-Organ Donors' (2008) 122 *Pediatrics* 454.

³⁰⁵ Styczynski and others (n 303).

³⁰⁶ Lainie Friedman Ross and J Richard Thistlethwaite Jr, 'Children as Living Donors', *Ethical Issues in Pediatric Organ Transplantation* (Springer 2016) 5.

³⁰⁷ *ibid* 6.

³⁰⁸ Wiener and others (n 302).

³⁰⁹ Ross and Thistlethwaite Jr (n 306) 6.

³¹⁰ Only fourteen Member States in the Council of Europe have ratified the Additional Protocol to the Convention on Human Rights and Biomedicine concerning Transplantation of Organs and Tissues of Human Origin, which requires protection of a donor such as child through a right to information (Article 12), the right to object (Article 14.v), and protection by authorization of a guardian (Article 14.iv). Chart of signatures and ratifications of Treaty 186, https://www.coe.int/en/web/conventions/full-list/-/conventions/treaty/186/signatures?p_auth=13GPIL37, accessed 4 January 2016.

informed consent and to fully understand the risks and harms. Because the donor does not receive any physical benefit from the donation, any harm to the child’s health, however slight, raises questions as to whether the donor child’s own right to *the highest attainable standard of health* may be compromised.³¹¹ Without an assurance that the child is actively and willingly choosing to participate in the process, pain and other physical side effects can impact the child’s *right to physical and psychological integrity*. This outcome may particularly result if the child feels silenced from emotional pressure to undergo the procedure, affecting *the child’s right to be heard*. Many of these problems may be amplified for children who are created purposely as “savior siblings”, who may learn that they were created for the sole or primary purpose of becoming a donor to an elderly sibling.³¹² Because the number of these children is unknown, concerns for their additional psychological suffering may be dismissed as speculative.³¹³ For all of these children, their *right to autonomy*, derived from the *right to private life* is likely implicated when they are not fully and freely choosing to participate in the decision to donate.

7.5 Summary of the rights at stake

Transplantation as a field of biomedicine is one where the right to life of children is at stake for potential recipients and donors, and for both classes of children as well as their right to the highest attainable standard of health. In some cases, the rights of these children may be pitted against each other. The diversity of interests of the affected children as a class – based on age and their interest in matters related to consent and the right to be heard – require careful consideration of whether a purely class-based analysis for all types of transplantations at all stages of life are appropriate for every condition. Given the scientific uncertainties at issue, questions remain whether greater scientific oversight and substantive standards should be required in clinical practice, rather than leaving these matters to professional standards and guidelines, and whether special protections for children in these circumstances are needed.

Scientific challenge/procedure	Rights at stake
Children as transplant recipients	<ul style="list-style-type: none"> • Right to the highest attainable standard of health • Right to informed consent • Right to be heard
Children as donors at death	<ul style="list-style-type: none"> • Right to life • Right to private and family life • Right to the highest attainable standards of health
Children as living donors	<ul style="list-style-type: none"> • Right to autonomy and private life • Right to physical and psychological integrity • Right to the highest attainable standard of health • The right to be heard • The right to informed consent

³¹¹ Ross, Thistlethwaite and others (n 304).

³¹² Allane Madanamoothoo, ‘Saviour-Sibling and the Psychological, Ethical and Judicial Issues That It Creates: Should English and French Legislators Close the Pandora’s Box?’ (2011) 18 European Journal of Health Law 293.

³¹³ Smith (n 83) 120.



8. End of life care

8.1 Introduction

Children generally are expected to outlive their parents. Many, however, die before they reach adulthood.³¹⁴ In 2014, around 18.8 thousand children died before reaching one year of age in the EU Member States alone.³¹⁵ When the death of children is foreseeable, clinical decisions require difficult choices in the use of biomedical interventions, many of which have become more intricate and challenging as science has increased hope that treatment may avert or forestall child mortality. Children suffering from life-threatening conditions can also receive sophisticated technological support that allows them to survive longer. The limits of these interventions, however, inevitably raise questions regarding the termination of treatment, shifting care decisions to the alleviation of suffering and management of pain. These questions often become less questions of science and much more deeply personal. In this sense, pediatric practice in many parts of the world today has become much more deferential to children in these circumstances than ever before – in many cases, recognizing their right to end treatment. When younger children are involved, however, biomedicine is continually tested as it is used to resolve questions that may not permit easy answers, such as how to know when an infant, especially a neonate, is in pain. Critical decisions default to parents and clinicians, who may not be able to scientifically determine the best interests of the child – including the decision of simply letting go of that child.

This chapter, perhaps more than any other in this report, reflects the limits of biomedical science in resolving matters in accord with children's rights, as the interventions addressed here vary considerably because of different cultural, religious, and legal judgments as to when certain biomedical interventions may be used. They also implicate the scope of authority of parents and the limitations on lawful medical practice. Thus, the chapter first turns to matters regarding withdrawal of active treatment, then to palliative care, before turning to assisted dying and the termination of life, where regulatory approaches control determination of their legality and the boundaries of scientific inquiry. Currently, there is neither consensus among European countries as to the acceptance of this last practice,³¹⁶ nor in its application to children. Only two nations – the Netherlands and Belgium – expressly permit such practices to be applied to children, and then only in some cases. In the former of these two, clinical practice appears to have extended assisted dying beyond the statutorily permitted scope, with tacit governmental approval for certain neonates. In all of the matters addressed in this chapter, it is not surprising, therefore, that medical and other authorities may invoke human rights to determine what should be the decisive factor in resolving these controversies.

³¹⁴ For example, according to the WHO data, in the WHO European Region the risk of death before turning 5 is (11 per 1000 live births). See WHO, http://www.who.int/gho/child_health/mortality/mortality_under_five_text/en/, accessed 18 November 2016.

³¹⁵ Mortality and life expectancy statistics. Eurostat, http://ec.europa.eu/eurostat/statistics-explained/index.php/Mortality_and_life_expectancy_statistics, accessed 17 November 2016.

³¹⁶ Joachim Cohen and others, 'Public Acceptance of Euthanasia in Europe: A Survey Study in 47 Countries' (2014) 59 *International Journal of Public Health* 143.

8.2 Withdrawal of active treatment

8.2.1 Scientific background

Determining when to withdraw active treatment for children who are likely to die has been described as one of the most difficult areas of pediatric practice. From a scientific point of view, many of the questions underlying these decisions vary according to the age of the child. Because the neonatal period and early infancy are critical phases of life for severely ill newborns, many decisions regarding continuing active treatment are complex, given that the array of potentially lifesaving interventions on fragile children themselves may be risk-laden and painful. Care decisions for neonates also occur in acute situations (often born in a state of medical crisis) and in labor wards, where parents who must make withdrawal decisions are particularly vulnerable.³¹⁷ The general clinical presumption in such cases is to attempt life-saving treatment first and then assess the validity of continuing treatment thereafter. These latter determinations can be difficult for matters involving children. Where children have lived with illness or have undergone considerable treatment, the critical point of futility may be highly subjective, depending not only on the child's physical condition or questions about the child's competence, but also on the child's emotions and aspirations to survive, all of which may be highly influenced by parents. Quality-of-life projections for neonates and infants, in contrast, are even more difficult, as input from the child is impossible and pain responses cannot be definitively measured.

Medical law, however, often determines when decisions to end care can occur, as failure to provide care that leads to the death of a patient may cross into other areas of law, such as criminal law. Many of these rules vary among jurisdictions as to when clinicians are required to offer treatment or permitted to halt it. These variations cannot be summarized here. Within these juridical bounds, clinical determinations under prominent guidelines combine human rights concerns with biomedical criteria for treatment withdrawal where life is limited in (1) quantity or (2) quality.³¹⁸ The first category includes assessments based on the determination of actual death, imminent death, or inevitable death in the absence of life-sustaining treatment. As noted in Chapter 7, decisions regarding the criteria for actual death in many children (brain or cardiopulmonary death) are scientifically controversial. Both imminent death and inevitable death determinations depend on questions of whether life-sustaining treatment will only prolong life for short periods of time without other benefits for the child, and, therefore, require biomedical estimations of when death is likely to occur. In the latter category, critical determinations are made on the basis of pain and suffering of the child from treatment or the child's physical condition, or whether the severity of the child's condition itself is considered sufficient to outweigh any benefit from preventing natural death. Though no known medical guideline appears to consider biomedical determinations dispositive in these inquiries, it is clear that they carry great weight when children cannot convey their own feelings of suffering.

8.2.2 Analysis

The juridical difficulty involved in questions of withdrawing treatment may be as difficult as the biomedical ones, as even medical guidelines recognize the conflict between *the right to life* of the child and the *right to physical and psychological integrity*, including *protection from inhumane and degrading treatment*. When children are able to express their suffering and wish to end treatment with parental support, the questions may be simpler to resolve. Refusal to honor the child's wishes in these circumstances would clearly violate the *right of the child to be heard* and *the child's right to*

³¹⁷ Vic Larcher and others, 'Making Decisions to Limit Treatment in Life-Limiting and Life-Threatening Conditions in Children: A Framework for Practice' (2015) 100 Archives of disease in childhood s1.

³¹⁸ *ibid* s7–13.

biological and psychological integrity, as well as violate a right of the child or the parents' *right to consent* to interventions questionable as treatment. Frequently, however, the clinical team determines that care is futile, but parents may wish the care to continue. Parents and clinicians may also seek to continue treatment over the child's objections. These questions, however, require considerable further legal analysis to determine how the matters will be resolved in different jurisdictions as a human rights matter. When clinicians and the child agree over parental objections, clinicians may be able to seek legal intervention to assist the child, protect themselves from liability, or help the parents understand that the child's wishes are in accord with biomedical science and compassion. Without a right of the child to consent, or access to a representative or legal authority for assistance, the ability of children to invoke and seek protection of their rights is unclear, much less their ability to contest biomedical assessments that favor the child's possibility of survival as allegedly outweighing the child's suffering.

8.3 Palliative care at the end of life

8.2.3 Scientific background

Generally, the transition from providing treatment to managing care can be challenging for all the parties involved.³¹⁹ Under international standards, palliative care for children, particularly the management of pain and suffering, is expected to occur from the beginning of diagnosis of illness, regardless of treatment.³²⁰ Toward the end of a child's life, such care is expected to provide support to the child and the family until death, though it also should not hasten death.³²¹ Implementing such care is not a simple matter. As the end of life nears or may be imminent, pain assessments may be especially difficult, depending on the condition of the patient, given that pain by definition includes any "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".³²² In order to appropriately manage the pain, clinicians first must attempt to assess it and then determine what treatment options exist. As with end-of-life determinations, the degree to which these determinations should be predominantly biomedical is unclear.

As suffering is regarded as a subjective feeling, it is difficult to measure scientifically.³²³ Though many medical guidelines dovetail with recommendations from the Committee on the Rights of the Child regarding assessing children's wishes through emotional and behavioral responses – even for young children – the assessments can be challenging because of the multitude of factors that could affect minors' reactions to pain. Conscious children who reach certain age thresholds can often communicate the level of their pain to a considerable degree.³²⁴ Very young children may scream and grimace because of fear, rather than pain,³²⁵ affecting their assessment. Children who cannot express their feelings in speech may only express themselves through crying, movements, adverse reaction to feeding, and similar behaviors.³²⁶ Furthermore, the expression of pain and the assessment of its intensity could also be affected by the child's condition; for

³¹⁹ J Randall Curtis and Gordon D Rubinfeld, *Managing Death in the ICU: The Transition from Cure to Comfort* (Oxford University Press 2000).

³²⁰ WHO Global Atlas of Palliative Care at the End of Life (2014) 5-6. According to the WHO, for children and all patients, "palliative care is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications".

³²¹ *ibid.*

³²² Kliegman and others (n 14) 360.

³²³ AA Eduard Verhagen, 'The Groningen Protocol for Newborn Euthanasia; Which Way Did the Slippery Slope Tilt?' (2013) 39 *Journal of Medical Ethics* 293.

³²⁴ Daniel S Tsze and others, 'Validation of Self-Report Pain Scales in Children' (2013) 132 *Pediatrics* e971.

³²⁵ Kliegman and others (n 14) 360–361.

³²⁶ Verhagen (n 323).

example, cognitively impaired children are commonly being regarded as being more sensitive to pain, which, in fact, could be misleading as a reflection of a need for pain medication.³²⁷ Children who are incapacitated but show signs of pain at all ages may be exceedingly difficult to assess for pain responses, particularly neonates, given that aggressive interventions needed to keep them alive are substantial, while even their ability to react physically may be minimal.

Scientific uncertainty exists over which pain medication to use as well. For managing pain, sedatives and analgesics can be used, such as opioids (fentanyl, methadone, morphine), and benzodiazepines (clonazepam, diazepam, lorazepam, midazolam).³²⁸ Here as well, however, there are considerable differences in clinical practice that cannot be explained by medical judgment alone. Much turns on parental influence and the reactions of the child. Though the WHO has assisted in the development of pain measurement and management scales, positions of neonatologists in end-of-life administration of analgesics and sedatives vary by country or region, often resulting from the influence of culture and local law.³²⁹ As some critics argue, attempts to standardize the approach through protocols could also thwart patient-centered care essential to sparing the patient suffering.³³⁰ Use of pain management and sedatives, in particular, however, has also sparked the discussions of dual effects – that is, that they could have an impact on the life expectancy of the recipient. While medical opinion on dual effect is unsettled and, to some experts, considered an exaggeration of risk, dual effect cannot be scientifically ruled out as a possibility of all pain medication for all children. In all of these ways, controversies over the quality of the relevant science persist. Though WHO guidelines emphasize that palliative care extends beyond medication, research on how family support for caring for the child could affect how pharmaceutical effectiveness is lacking, particularly as to whether better pain management could occur through more holistic familial support.

8.3.3 Analysis

Palliative care remains a poorly understood aspect of the right to health for all children. Medical guidelines are clear that it should include a wide range of support for the child and the family – one that recognizes that care extends beyond the technological or pharmacological, but includes psychological, social, and holistic medical support for families of care for these children. Failure to provide that support thus undermines the child's *right to family life*. Guarantees for support and treatment options are particularly important for all children, as many child deaths occur outside a hospital setting, which is often favored by children and their families. Indeed, when offered with proper support, the proportion of hospital deaths appears to decrease.³³¹ The failure of health care systems to ensure that children receive palliative care thus relates to the freedom from *inhumane and degrading treatment* as well as the care of the whole patient, not just the illness, to protect both *the right to the highest attainable standard of health* and the *right to family life*. To the extent that pharmacological management carries any risks of hastening death, it implicates the *right to life as well*. In all of these ways, the obligation of states to consider the medical, healing aspects of biomedicine in fulfilling their positive obligations to the child are essential.

³²⁷ Kliegman and others (n 14) 361.

³²⁸ Kanecia O Zimmerman and others, 'Sedatives and Analgesics Given to Infants in Neonatal Intensive Care Units at the End of Life' (2015) 167 *The Journal of Pediatrics* 299.

³²⁹ *ibid.*

³³⁰ *ibid.*

³³¹ Finella Craig and Alexandra Mancini, 'Can We Truly Offer a Choice of Place of Death in Neonatal Palliative Care?' (2013) 18 *Seminars in Fetal and Neonatal Medicine* 93.

8.4 Assisted dying practices

8.4.1 Scientific background

In most European jurisdictions, actively facilitating the death of another person is not permitted. Though withdrawing active treatment and the use of pain medication in clinical settings may be conceptually and legally separate from intentionally hastening death, advocates of assisted dying have argued that these actions, too, are affirmative steps for critically ill persons that lead to death, the principles behind which should extend to assisting those who are suffering from such conditions and likely to die soon.³³² Others have questioned whether assisted dying medicalizes what would otherwise be a crime.³³³ In the European regulatory arena, only a few states provide for a legal framework that may be interpreted clearly to permit assisted dying practices.³³⁴ Two nations – the Netherlands and Belgium – explicitly allow for the active facilitation of the termination of the life of some children in clinical practice settings using biomedical interventions.³³⁵ These regulatory frameworks demonstrate the considerable difficulty, if not impossibility, of disentangling biomedical questions from legal ones in this subject area.

In the Netherlands, euthanasia of those older than 16 years (and in exceptional cases of those starting from 12 years of age) has been available for more than 20 years.³³⁶ For a considerable period of time, neonatal euthanasia has also been permitted. Outside of the statutory framework, clinicians at the University of Groningen Medical Center developed a protocol in concert with public officials – known as the Groningen Protocol – to regulate the practice of actively ending the life of newborns and to prevent uncontrolled and unjustified killing.³³⁷ As a result, in the Netherlands, infants and newborns may be euthanized if they (a) have no chance of survival; (b) have a very poor prognosis and are dependent on intensive care; or (c) are predicted not to be dependent on intensive care but are expected to have poor quality of life, associated with sustained suffering, and at risk of being subjected to nonmedical euthanasia.³³⁸ The chief architects of the Protocol have acknowledged that assessment of pain and suffering “is a subjective feeling that cannot be measured objectively, whether in adults or an infant” but claim that “experienced caregivers and parents are able to evaluate the degree of suffering in a newborn” using pain “scales” – assessments of vital signs and “observed behavior”.³³⁹ Reported use of the protocol over several years indicates that children with epidermolysis bullosa and spina bifida have been clinically euthanized; 15 infants in the latter category were euthanized, but reported euthanasia for such infants dropped to zero over time, for reasons that are not clear.³⁴⁰

More recently, in 2014, Belgium’s Parliament approved an amendment of the 2002 Belgian Act on Euthanasia to allow euthanasia for chronically ill children. It permits euthanasia for children who are experiencing constant and unbearable suffering. Unlike in the Netherlands, Belgian law requires (1) that the child faces constant and unbearable suffering; (2) that the child voluntarily

³³² Verhagen (n 323). On the legal requirements *see* the Termination of Life on Request and Assisted Suicide (Review Procedures) Act.

³³³ Those embrace euthanasia, physician assisted suicide and assisted suicide. Relatively recently, death has also been medicalized, labeling it as medical aid in dying (Quebec, Canada). *See* Kavot Zillén and Santa Slokenberga, ‘Medical Aid in Dying in Quebec—legal Considerations’ (2014) 2 *Journal of Medical Law and Ethics* 109.

³³⁴ Nicole Steck and others, *Euthanasia and Assisted Suicide in Selected European Countries and US States* (2013) 51 *Medical Care* 938.

³³⁵ The Dutch Termination of Life on Request and Assisted Suicide (Review Procedures) Act. The Belgian Act on Euthanasia.

³³⁶ Verhagen (n 323). On the legal requirements *see* the Dutch law (n 335).

³³⁷ Eduard Verhagen and Pieter JJ Sauer, ‘The Groningen Protocol — Euthanasia in Severely Ill Newborns’ (2005) 352 *New England Journal of Medicine* 959.

³³⁸ Verhagen (n 323).

³³⁹ Verhagen and Sauer (n 337).

³⁴⁰ *ibid.*

consents to and explicitly requests euthanasia, and (3) that the child’s parents consent. It excludes access to euthanasia for children with an intellectual disability or mental illness,³⁴¹ as well as those unable to express their request because of their age, such as newborns.³⁴²

8.4.2 Analysis

The recent developments in Belgium and the Netherlands alone demonstrate some of the difficulties associated with assisted dying for minors. On the one hand, the *right to autonomy* of minors could be said to be enhanced by access to it, as well as their *right to be heard* and their *physical and psychological integrity*. All of these same rights could be at risk when biomedical decisions are in error, jeopardizing the child’s *right to life* as well. Distinctions made in the aforementioned legislation raises the question as to the scientific foundation of granting some children access to assisted dying, but not others, as well as non-legislative protocols that rest on the clinical belief that subjective suffering can be determined for neonates on the basis of variable criteria. To the extent that expansion of these measures is encouraged, multidisciplinary input should be required to determine the limits of science and its effects on the rights of the children involved.

8.5 Summary of the rights at stake

End-of-life care in children must be individualized for the needs of the patient, as is true for all care. In this field, however, the limitations of science should trigger a rights-based approach to determining how this care is deployed. For withdrawal of treatment and pain management, medical guidelines give substantial weight to the child’s suffering and need to be heard, but these interests also directly correspond to well-established rights of the child. Palliative care requires consideration the overall situation of a family and providing family-centered care as part of the child’s right to private and family life. These matters illustrate that human rights and medical guidelines overlap and can inform each other, rather than being seen as in conflict. Instead, both should be considered essential to providing children adequate and respectful care.

Scientific challenge/procedure	Rights at stake
Withdrawal of active treatment	<ul style="list-style-type: none"> ● Right to be heard ● Right to privacy ● Freedom from inhumane and degrading treatment ● Right to life
Pain management	<ul style="list-style-type: none"> ● Right to the highest attainable standard of health ● Right to life ● Right to family life ● Freedom from inhumane and degrading treatment
Assisted dying practices	<ul style="list-style-type: none"> ● Right to life

³⁴¹ Andrew M Siegel, Dominic A Sisti and Arthur L Caplan, ‘Pediatric Euthanasia in Belgium: Disturbing Developments’ (2014) 311 JAMA 1963.

³⁴² Bernard Dan, Christine Fonteyne and Stéphan Clément de Cléty, ‘Self-Requested Euthanasia for Children in Belgium’ (2014) 383 The Lancet 671.



9. Summary and Conclusions

9.1 Overarching concerns for children's rights in biomedicine

This report documents the existence of multiple biomedical interventions in a range of settings that affect children across their developmental stages, with risk not only of physical or psychological harms but also to children's rights. Based on a considerable survey of scientific and medical literature, the report identifies developments that raise concerns in these areas – both within emerging sciences and technologies, such as assisted reproductive technologies and genetic testing and enhancement, as well as in pediatric health care. In clinical settings, many questionable practices have lingered long after patient complaints and evidence-based reviews have challenged their safety and efficacy, whereas even those that provide necessary treatment often come with a lack of long-term data that may be necessary for minors or their parents to give truly informed consent, especially when treatment options are available. Thus, this report should raise questions as to why uncertainties surrounding so many biomedical interventions on children have not triggered greater governmental recognition of the need for oversight to protect children's rights.

Indeed, the lack of sound data regarding many biomedical interventions affecting children requires special attention. Scientific uncertainty in biomedicine affecting children should be expected, as noted at the outset of the report, because of the difficulties of conducting research on children – whether in minimizing research risks or burdens or predicting whether proposed interventions will benefit them. Throughout this report, however, much of the medical literature cited reflects candid acknowledgments that ongoing practices lack scientific support or that the causes of adverse effects on children from interventions are poorly understood. Given that even more severely negative outcomes are almost certainly not reported in the literature and that much of the reported data cannot be verified, any authority concerned for the rights of children should be concerned as much by what is *not* known as by what is known, especially as many known troubling practices have not been stopped in the wake of scientific skepticism and criticism.

This report should cast no doubt on the good intentions of clinician-researchers who wish to develop the most scientifically advanced care to promote the health of children. It should also not be seen as a call to overhaul regulation of clinicians or any particular reform. Rather, the different rights of children that are identified in this report may require tailored responses under regional or international human rights frameworks. For example, under the European Convention on Human Rights, Contracting States have a narrow margin of appreciation in determining how to protect certain rights of children, such as those related to identity and intimacy, and are also required to have specific remedies for physical and psychological harm to children.³⁴³ In protecting individuals from scientific uncertainty in biomedical practices, including health care, states must have an adequate legal framework to protect individuals, but also have a wider margin of appreciation – and thus discretion – to intervene in biomedical practices relative to the risks in biomedicine.³⁴⁴ Accordingly, a critical question this report should raise is whether deferential approaches to regulating biomedical practices, including clinical practices, are

³⁴³ See, e.g., case *Söderman v. Sweden* [GC], App no 5786/08, 12 November 2013, paras 79-86.

³⁴⁴ See, e.g., case *S.H. and others v. Austria* [GC], App no 57813/00, 3 November 2011, para 97.

warranted in individual areas of biomedicine, or whether clarification is needed of the rights of children, as well as national obligations to protect children from risks of rights violations.

This report, however, remains a survey, one conducted over limited duration. Each of the chapters in this report would benefit from an in-depth investigation of the practices identified, as would many others that could not be covered here. Of great concern, in fact, has been the difficulty to determine what actual practices are in the 47 Contracting States of the Council of Europe or even in a majority of those states. Many reports from regional authorities and human rights investigators themselves provide anecdotal data, without detailed documentation and scientific support for their findings. Greater information, therefore, is necessary to determine where sustained oversight of scientific advances and uncertainties in biomedicine are needed most, especially the extent to which they affect the rights of children.

With this in mind, this chapter concludes by identifying potential rights at stake for children in biomedicine, or where obligations to provide protection may need to be clarified or improved in a biomedical context. The CRC remains a fundamental guide for these considerations, as it specifically recognizes the human rights of children, framed by the interests of the whole child and protection of the child's human dignity.

9.2 Rights identified

9.2.1 The highest attainable standard of health

Most of the issues addressed in this report relate to the child's right to highest attainable standard of health, recognized in Article 24 of the CRC. In addition to this, Article 6 of the CRC stresses that states parties shall ensure to the maximum extent possible the survival and development of the child, indicating their obligations to take all possible measures to improve healthcare for newborns, reduce infant and child mortality, and create conditions that promote the well-being of all young children during this critical phase of their lives.³⁴⁵ The survival and physical health of infants and children are prioritized, since proper prevention and intervention strategies during early childhood have the potential to impact positively on young children's current well-being and future prospects. As this study emphasized from the outset, however, ensuring the highest attainable standard of health for each child requires an understanding of the risks each child faces, which often varies at several stages of development. Many of the risks to children noted in the report reflect a lack of caution in biomedical practices, with questionable interventions on neonates, infants, young children, and adolescents surfacing even in pediatric clinical practice.

This report was intended to emphasize that many biomedical interventions, both inside and outside the clinical context, pose risks to children, even intervening on behalf of future children before their rights attach. Many different types of advances in biomedicine and new technological developments have been offered to prospective parents with the hope of creating a healthy child or to diagnose and treat the condition of the unborn child at an early stage of development. These technologies and methods – such as IVF and mitochondrial donation, non-invasive prenatal genetic testing, and different types of genetic enhancements – by design are directed toward the health and wellbeing of the future child, ideally unaffected by genetic disorders and conditions. These procedures may be seen as having the character of preventive medicine, which is an important feature of the right to health. But while these technologies enable individuals to create children free from genetic disorders, they also introduce scientific and legal challenges in relation to the future child's right to health – taking into account the scientific uncertainty about

³⁴⁵ Committee on the Rights of the Child, General comment no 7 (n 2), para 8–10.

all the risks involved, for example in relation to ART and interventions *in utero*. Genetic testing of questionable utility and validity also raises similar concerns, particularly as the tests may be done without the child's awareness or certainty that any testing – correct or otherwise – might lead parents to seek unnecessary care.

With regard to clinical practice, assurances of benefit maximization and risk minimization were not easy to identify in many cases. This was especially so for treatment of children who are critically ill, suffering from serious mental health disorders, or with needs for transplantation. It also includes interventions where the risks are highly variable and uncertain and the overall benefits to the child are not easy to confirm – for example, where short-term survival is difficult to project, or where control of the social effects of mental health conditions appear to be the aims of interventions. Other children appear at risk where highly invasive treatment is predicated on claimed psychological benefit or backed by questionable data, such as procedures to “normalize” them. The continuation of these interventions without substantial evidence of safety, efficacy and benefit should raise considerable alarm where the health of children is concerned.

9.2.2 Physical and psychological integrity

Many challenges in relation to children's right to health overlap with other closely connected rights, such as their right to physical and psychological integrity, protected in numerous international human rights instruments. For example, the European Court of Human Rights has established that the protection of private life in Article 8 of the ECHR encompasses the physical, moral and psychological integrity of a person. Furthermore, each child's right to respect for human dignity and physical and psychological integrity is to some degree recognized (indirectly) in Article 19 of the CRC. That provision stipulates Contracting States' obligation to protect the child from all forms of physical or mental violence, injury or abuse, neglect or negligent treatment, maltreatment or exploitation, and the like. The term violence in the provision represents *all* forms of harm to children, also including non-physical and non-intentional harm.³⁴⁶ The Committee on the Rights of the Child has thus clarified that each child has an absolute right to physical and psychological integrity as a matter of human dignity.³⁴⁷ Accordingly, the child's right to integrity is interconnected with the protection of the child's right to be respected and protected as a rights holder and as a unique and valuable human being with an individual personality and distinct needs and interests.³⁴⁸

One barrier to applying these rights in a biomedical context – particularly in clinical practice – has always been the presumption that parents and clinicians make decisions in the best interests of their children to promote their physical and psychological integrity. As this report has shown, the presumption, however valid generally, is more problematic than might be believed. In the context of ART and genetic testing, parents who consent to interventions may have their own interests at stake or may not fully foresee the risks to the children. Similar problems may arise in transplantation, where parents may ask one child to take risks for another or consent to aggressive care for another child's sake, decisions that these children might not make for themselves. In many cases, parents' favor for interventions raises questions as to whether their struggles with their children's differences, appearances, or behavior may make them more ready to consent to invasive treatments with questionable benefits for those children.

As with exploring the right to the highest attainable standard of health, interpreting the rights to physical and psychological integrity may require raising standards for clinical practice, extending

³⁴⁶ Committee on the Rights of the Child, General comment no 13 (2011), CRC/C/GC/13.

³⁴⁷ *ibid.*

³⁴⁸ *ibid* para 3.

human rights obligations to many private actors and balancing protections of the children with the rights of parents to consent. The limits of parental and clinical authority, indeed, may need to be more precisely mapped.

9.2.3 Consent and due consideration for the child's views

Issues relating to children's ability to participate in decisions regarding their health and wellbeing are crucial in the biomedical field, particularly to respect their basic human dignity. Article 12 of the CRC protects the child's right to form his or her own views and the right to express those views in all matters affecting the child. In health care, this requires allowing children to express their views and to participate in their own development where possible. Though the right may be generally recognized in national legal orders and protected by other human rights instruments, the right to consent and to receive information in biomedical contexts, especially health care, is often legally attached only to the parents. Unlike the context of research – where interventions must be stopped if the child objects – no such categorical right extends to other biomedical interventions, even when clinical treatments in practice may be invasive, lacking in scientific support, or used in practice without long-term data, rationalized on the grounds that no effective treatment exists.

Many human rights authorities have proposed that children *should* be involved in many decisions relating to their health and *should* be given information about proposed treatments and their effects and outcomes. So, too, they recommend that children's consent *may* be obtained and their views *should* be given due weight when unnecessary medical or surgical treatments are carried out, even though it might result in a delay of the procedure until the child can fully consent. It is unclear, however, when these aspirations may be compulsory under human rights instruments – or whether they should be mandatory, for example, when the child is in pain, when the treatment could be delayed, or when the child's safety, dignity, and rights are at stake.

9.2.4 Identity and private life

The child's rights to identity and private life are only abstractly set forth in many human rights instruments, such as Article 8 and 16 of the CRC or Article 8 of the ECHR. Many authoritative interpretations, however, have given them considerable content. The Committee on the Rights of the Child, for example, has noted that when the right to identity is considered, the child's gender, sexual orientation, and other aspects of personality should be considered.³⁴⁹ So too has the Committee emphasized that the child's right of privacy extends to medical information and the ability to seek confidential medical advice. Thus, the child's right to access information can flow from the right to identity in other contexts, such as Article 7.1 of the CRC, providing for a right to know one's parents - as the Committee has previously stressed that a child's possibilities to access that biological information is in the best interest of that child.³⁵⁰

Many interventions identified in this report intersect with both the right to identity and right to private life, such as in the protection of children's genetic information of children, as well as for protection of those children whose gender or sexuality has been targeted with invasive medical procedures. Human right authorities may require greater precision and clarity in setting forth the content of the rights to fully protect the private life and identity of children, particularly in light of the free development of their personality.³⁵¹ The lack of an explicit, well-established right to a

³⁴⁹ Committee on the Rights of the Child, General comment no 14 (2013), CRC/C/GC/14, (V.A.1), para 55.

³⁵⁰ *ibid* para 56.

³⁵¹ Bart Van der Sloot, 'Privacy as Personality Right: Why the ECtHR's Focus on Ulterior Interests Might Prove Indispensable in the Age of Big Data' (2015) 31 *Utrecht Journal of International and European Law* 25. Kirsty Hughes, 'Child's Right to Privacy

gender identity or sexual identity, for example, may explain why parents and clinicians have freely been able to use biomedical interventions to attempt to shape and suppress those identities when full equality for adults in this area has yet to be recognized.³⁵² The natural access of parents to much intimate information about their children, especially in health care, leaves many questions open about the scope of the right of children in biomedical contexts.

Indeed, with regard to these rights, in particular, technology may push or cross the bounds of identity rights in ways that are difficult to foresee. As ART and other technologies creating future children become more advanced, the complexities of a child's identity, and what parents and their service providers are willing to reveal, may have an effect on the child's right to an identity, even if it yields no information essential to the child's health or future. Genetic testing may further implicate the child's right not to know certain aspects of its identity, particularly as genome sequencing – justified on the basis of its health – may collect far more information than the child would want and lead to new forms of gene editing and other therapies that affect the dignity, identity, and autonomy of the child. In all of these ways, the scope of the right to identity will remain critical to the degree of protection afforded to children against scientific advances and uncertainties.

9.2.5 Protection from discrimination

Children may be seen as particularly at risk of discrimination because they are relatively powerless and depend on others for the realization of their rights, perhaps even more so when they are considered to have a status that has historically been the basis of discrimination and disparate treatment.³⁵³ The right to protection against discrimination enshrined in Article 2 of the CRC ensures the protection of each child from discrimination on any status.³⁵⁴ This includes discrimination on the basis of sex and disability, both of which are expressly mentioned in Article 2. As with the right to identity, however, the full protection of these rights may be questioned: protections on the basis of “sex” and gender are increasingly prioritized for formal equality between the class of “men” and “women”, but discrimination on the basis of sex characteristics and gender for minorities is not fully recognized. Persons with disabilities are often considered to warrant special treatment for their benefit, which is often used, in turn, to justify interventions on their behalf. Children with mental health disabilities, for example, are restrained and medicated on this very basis.

Discrimination on the basis of sex and disability has surfaced in multiple interventions mentioned throughout this report, from growth suppression on girls that are “too tall”, to sex selection in ART and from interventions *in utero* and infancy to eliminate differences in sex development, to a long history of invasive and adverse treatments on lesbian, gay, bisexual and transgendered youth. Similar interventions have emerged for children with disabilities. The expectations raised by ART to screen out disabilities puts future children born with those disabilities at risk of stigmatization as well as parental rejection. Genetic testing to screen for disabilities may create perceptions of disability from probing the child's genetic makeup. Children with physical disabilities also appear to be subject to surgical and hormonal interventions – to stunt their growth or even reshape

and Article 8 European Convention on Human Rights' in Michael Freeman (ed), *Law and Childhood Studies: Current Legal Issues*, vol 14 (Oxford University Press 2012).

³⁵² The Yogyakarta Principles, for example, recognize rights for sexual and gender minorities in biomedicine in particular that have yet to be universally recognized, for example, in biomedicine, in Principles 17 & 18. Michael O'Flaherty, 'The Yogyakarta Principles at Ten' (2015) 33 *Nordic Journal of Human Rights* 280. For more information, see Yogyakarta Principles, <http://www.yogyakartaprinciples.org/>, accessed 4 January 2017.

³⁵³ Committee on the Rights of the child, General comment no 7 (n 344), para 5.

³⁵⁴ Jaime S King, 'Predicting Probability: Regulating the Future of Preimplantation Genetic Screening' (2008) 8 *Yale journal of health policy, law, and ethics* 283, 58.

them with cosmetic surgery, purportedly for their own benefit but with considerable concern that the treatment is designed with their parents' interests in mind. The science behind many psychiatric and psychological diagnoses for children with disabilities, as well as the safety and benefit of interventions on their behalf, are not well documented. The need to reconsider whether they are forms of discrimination remains great.

9.2.6 Liberty and protection from inhumane and degrading treatment

The prohibition of torture is one of the few absolute and non-derogable human rights recognized in both regional and international human rights instruments, such as in the UN Convention against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment, Article 5 of the Universal Declaration of Human Rights, Article 7 of the International Covenant on Civil and Political Rights and Article 3 of the ECHR. The European Court of Human Rights' case law indicates that only "severe" pain or suffering may constitute cruel and inhuman treatment, but that is not the case for degrading treatment. In the case of such treatment, the severity depends on the specific circumstances, in which special attention is given to the duration of the treatment, its physical and mental effects and, in some cases, the sex, age, and state of health of the victim.³⁵⁵ These considerations are relevant to health care, especially concerning treatment and handling of children, who naturally are placed in a vulnerable position. These considerations are also frequently intertwined with the liberty of the child.

Many treatments described in this report already have been criticized by human rights authorities on these grounds – including denial of palliative care and treatment for pain, involuntary hospitalization and invasive treatments for psycho-social disabilities, forced mental health therapies on children, "reparative" therapies to change gender identity and sexual orientation, and removal of genitals and gonads of children with differences in sex development and intersex conditions.³⁵⁶ But many others have not, such as whether governments, clinicians, and parents can force a child to endure repeated painful therapies – whether standard or innovative – or to undergo prolonged, traumatic after-care or not to be able to consent to the withdrawal of life-sustaining care. Unfortunately, as seen in the case of children with differences in sex development and intersex conditions, clinicians have not responded well to charges of torture, raising questions of whether to be effective, the right must be reformulated in a medical context, with a biomedical audience in mind.

9.2.7 The right to life

The right to life protected in various human rights instruments, such as Article 2 of the ECHR, is the most basic human right, which, similar to the prohibition of torture, may not be subjected to derogations. The right concerned imposes positive obligation on States to protect patients' lives and to ensure an effective independent judicial system to be set up so that the cause of death of patients can be determined. Questions related to children's right to life have in particular been raised in chapter 7 and 8 of this report. While the demand and need for tissues and organs are growing, the availability of these tissues and organs for children is decreasing. Consequently, children may be more likely to die waiting for transplantation than adults, because fewer organs are available that potentially could have been harvested from siblings, affecting their right to life. At the same time, the right to life may also be at stake when the risk involved in the transplantations procedure are high and may jeopardize the life of the recipient. So, too, the right to life has been implicated in relation to various end-of-life practices that allow terminating life,

³⁵⁵ Case *Jalloh v. Germany*, App no 54810/00 [GC], 11 July 2006, para 109.

³⁵⁶ Juan Méndez, Report of the Special Rapporteur on torture and other cruel, inhuman or degrading treatment or punishment, A/HRC/22/53 (2013).

taking into account that acts to deliberately end one's life, especially of the minors, are highly controversial.

9.3 The future of children's rights in an evolving biomedical landscape

Even though all of the procedures and technologies described in this report do not necessarily represent new legal challenges in the field of biomedicine and human rights, this study shows that many have consequences for children's rights both as currently formulated and also perhaps not previously imagined. The issues addressed are, at least to some degree, familiar ones for human rights law and practice – the right to private life, to health, to physical and psychological integrity, and the like. Many of these rights are all fundamental rights that are frequently described, discussed and referred to in the field of biology, medicine, and biomedical research. However, as it has been shown, the current use of questionable and unproven treatments in pediatric care and the expanded use of new technologies outside the clinical context – such as in the field of assisted reproduction and genetic testing – raises profound questions as to how the rights of children can be protected, perhaps inevitably leading to renewed discussions of the need for a European human rights instrument specifically aimed at children in the field of biomedicine.

The rights of children in the biomedical sphere are protected very generally and scattered across some core international and regional human rights treaties dealing with the rights of disadvantaged groups. Thus, one question that remains unanswered is whether there is a need for a human rights treaty that offers children a tailored, comprehensive and binding protection of their rights in the biomedical sphere – much as the Yogyakarta Principles, in the context of sexual orientation and gender identity protections, focused on medical rights and protections from medical abuses. The answer is not, however, straightforward. The current human rights frameworks, such as the CRC and Convention on Human Rights and Biomedicine, do recognize children's right to health, but they do not directly call for special protection in relation to medical experimentation and scientifically risk-laden or uncertain treatment outside of research settings. There is also no explicit reference to the child's right to informed consent in many instances.

The absence of a clear and comprehensive instrument that addresses bioethical concerns in relation to children may reflect difficulties in reaching a consensus on the matter. In the future, especially with the rise of new technologies, it may be necessary to re-conceptualize the rights for children in order to grasp how traditional the biomedical sciences operate in relation to children. Of equal importance, new rights formulations may require special focus on clinical practice – wherein so many decisions are based on empathy and experience and working with patients – and where scientific methods and standards, as well as law, are both sometimes considered to interfere with health care and professional judgment.

Future assessments of children's rights in biomedicine, therefore, may be challenging and require considerable collaboration. The absence of consensus regarding biomedical practices carried out on children among the Council of Europe's Member States may make it difficult to develop a regulatory framework for controlling and supervising these practices on a regional or international human rights level, which merits separate discussion. What remains to be done at this point, however, is to continue to raise awareness of the potential human rights violations that may occur due to the usage of these treatments and technologies from the perspective of the rights of the child, perhaps in ways that inspire reformulation of professional standards that are in accordance with those rights, either within current human rights frameworks or with new frameworks forming, at least for now, in the imagination.

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