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EU Regulatory Responses to Medical Machine Learning in Pediatric Care: A Missed Opportunity to Overcome a Therapeutic Gap?

1   Introduction

The child's right to health has the same four core components, as anyone else's right to health – availability, accessibility, acceptability, and quality of medical care.[1] The right to health,[2] coupled with the right to enjoy the benefits of scientific progress and its applications,[3] is supposed to incentivize states to further the development of medical care and ensure that children as a group, at least in theory, do not lag behind, and that when the care is rendered available to children, it is of appropriate (and proven) quality. Reality, however, can be rather different. For years, children in general and different specific pediatric patient groups have been marginalized by being subject to "adjusted", more commonly known as

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[1] See UN General Assembly, International Covenant on Economic, Social and Cultural Rights (ICESCR), 16 December 1966, United Nations, Treaty Series, vol. 993, p. 3, article 12 and UN Committee on Economic, Social and Cultural Rights (CESCR), General Comment No. 14: The Right to the Highest Attainable Standard of Health (Art. 12 of the Covenant), 11 August 2000, E/C.12/2000/4, para. 12; UN General Assembly, Convention on the Rights of the Child, 20 November 1989, United Nations, Treaty Series, vol. 1577, p. 3, article 24 and UN Committee on the Rights of the Child (CRC), General comment No. 15 (2013) on the right of the child to the enjoyment of the highest attainable standard of health (art. 24), 17 April 2013, CRC/C/GC/15, para. 112.
[2] ICESCR (n. 1) article 12.
[3] ICESCR (n. 1) article 15(1)(b).

off-label, medical care. While it is not necessarily a synonym to substand-ard care, quality concerns in off-label care are not foreign.[4]

Artificial intelligence (AI), including its subtype, machine learning (ML), has been labelled as "the most transformative technology" of the 21st century,[5] and is commonly hailed as a potential cure for many of the world's grave problems. AI, and in particular its subtype, medical machine learning (MML) holds the potential to transform medical care in general,[6] and pediatric medical care as its subset.[7] In addition to the tangible benefits of improved care to particular patient groups, considerable economic gain for the public health systems is forecasted.[8] Currently, considerable research initiatives are being funded to further the availability of high-quality medical care.[9] The pediatric patient population is one of the potential beneficiaries of these advances. This benefit could take place not only in terms of developing new and better diagnostic tools and cures, but also in terms of moving beyond the long-existed practices of adapting the adult patient studies and tailored outcomes for the pediatric group or subgroups therein and adjusting the therapies to match the medical needs of "smaller bodies", at least with respect to medical devices.

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[4] See in that regard Santa Slokenberga, 'The Standard of Care and Implications for Paediatric Decision-Making: The Swedish Viewpoint' in Clayton Ó Néill and others (eds), *Routledge Handbook of Global Health Rights* (Routledge 2021).

[5] Daniel Schönberger, 'Artificial Intelligence in Healthcare: A Critical Analysis of the Legal and Ethical Implications' (2019) 27 International Journal of Law and Information Technology 171, 171.

[6] Although in medical care any of the mentioned techniques could be of relevance, often ML is singled out as a technique of particular importance in healthcare. Danton S Char, Nigam H Shah and David Magnus, 'Implementing Machine Learning in Health Care—Addressing Ethical Challenges' (2018) 378 The New England journal of medicine 981. Jenna Wiens and others, 'Do No Harm: A Roadmap for Responsible Machine Learning for Health Care' (2019) 25 Nature Medicine 1337. S Dolley, 'Big Data Solution to Harnessing Unstructured Data in Healthcare' [2015] IBM Report.

[7] Keeley LaForme, 'How Machine Learning Experts and Physicians at Johns Hopkins All Children's Are Working Toward a Hea' <https://www.hopkinsallchildrens.org/ACH-News/General-News/How-Machine-Learning-Experts-and-Physicians-at-Joh> accessed 6 September 2021.

[8] European Commission. Joint Research Centre. and E Gomez Gutierrez, 'Artificial Intelligence in Medicine and Healthcare: Applications, Availability and Societal Impact.' (Publications Office 2020) 13 <https://data.europa.eu/doi/10.2760/047666> accessed 6 September 2021.

[9] See section 3.

While AI applications in medicine are already a clinical reality in modern medicine, its peak generally and in pediatric medicine specifically is yet to be achieved. To enable the potential of MML to transform pediatric medical care, adequate preconditions that further scientific research in the field and lead to qualitative pediatric care need to be in place. Member States of the EU are, to a considerable degree, preempted from acting on their own in the field. The EU regulates two central elements pertaining to pediatric MML – data protection and medical devices – , and in a near future, it is expanding its regulatory grip to capture another dimension, the artificial intelligence component. Thus, even if the Member States had an interest in taking greater steps in the field, those steps would need to be subordinated to the EU preemptive actions in the field.

This contribution aims to examine the legal preconditions for developing MML tools in pediatric medicine that are set forth within the EU law. It begins by reflecting in greater detail on the AI and MML potential to transform health care generally and pediatric care as a marginalized healthcare area specifically. Thereafter, it moves on to charter key areas of EU law of relevance to the development of pediatric MML devices. Finally, it synthesizes the findings and reflects on the EU legal preconditions and the potential to overcome a gap in pediatric medical care through advancing pediatric MML. I argue that considerable steps have already been taken in order to ensure that qualitative MML medical devices for pediatric care are placed on the market, but whether these will lead to high-quality products in the field will depend on a number of considerations, including the national application of the harmonized EU requirements. I argue that none of the surveyed legal instruments, regulating data protection, medical devices and AI, contribute to furthering the development and availability of the devices directly and thus the EU misses a chance to contribute to reducing the therapeutic gap in pediatric medical care.

2 AI, MLL, medical care and pediatric medicine

AI has been broadly defined as the "science and engineering of making intelligent machines".[10] ML is a particular technique of data analytics. It can be used to develop algorithms that can learn, identify patterns, and act on the available data.[11] One central aspect of machine learning is the availability of adequate data for the algorithm to learn without being programmed to reach a particular conclusion. The learning may be either supervised or unsupervised.[12] In the former, humans label the data used to train and validate an algorithm in advance, whereas in the latter the algorithm learns patterns from unlabeled data.[13] Depending on the design, ML algorithms can be divided into two groups, the locked ones that are unable to develop themselves further and the adaptive ones that could continuously learn from data and optimize their performance.[14] The ability to learn from real-world use and experience and the capability to improved ML performance has been highlighted as one of the greatest benefits of the technology for the field of medicine.[15]

AI applications in medicine are not a novelty. The initial efforts, that date back to the 1960s, focused on diagnosis and selection of the most appropriate therapy. A prime example of such technology is a computer-based consultation technology in clinical therapeutics, the MYCIN system developed in 1972 at Stanford University. This system was developed using clinical decision criteria acquired from experts to advise

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[10] 'What Is AI? / Basic Questions' <http://jmc.stanford.edu/artificial-intelligence/what-is-ai/> accessed 6 September 2021.

[11] Rohan Bhardwaj, Ankita R Nambiar and Debojyoti Dutta, 'A Study of Machine Learning in Healthcare', *2017 IEEE 41st Annual Computer Software and Applications Conference (COMPSAC)* (2017) 237.

[12] However, technically, more nuanced approaches exist, see Batta Mahesh, 'Machine Learning Algorithms-A Review' (2020) 9 International Journal of Science and Research 381.

[13] Mahesh (n. 12).

[14] Food and Drug Administration, 'Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) - Discussion Paper and Request for Feedback'.

[15] Food and Drug Administration, 'Artificial Intelligence and Machine Learning in Software as a Medical Device' <https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device> accessed 4 October 2021.

physicians concerning the antimicrobial therapy section.[16] While this particular system was never used in clinical care, it was one of those contributing to furthering public interest in the field by the early 1980s, along which followed commercial interest and funding for the field.[17] However, similarly as in other fields, also in the field of medicine, AI winter came, considerably affecting interest and slowing down the field.[18] Today, new applications and startups in the field emerge on a daily basis,[19] in the aspiration to harness the benefits that the technology holds.

Building on the steady progress in the field, in the last decades, AI in medicine, and in particular MML has considerably evolved. Researchers are actively pursuing opportunities to realize the AI potential throughout all aspects of care in order to enhance and improve patient care, for example, through improved accuracy and efficiency of diagnostics, selection of therapies and prediction of outcomes.[20] There are high expectations that the field will considerably accelerate and, while caution also exists, there is considerable awareness of the importance of the technology in future medical care.[21]

Largely, AI applications in healthcare can be clustered in the following three groups: predictive use, diagnostic use and clinical decision-making aid. Predictive use of MML refers to setting a prognosis for an individual patient. Diagnostic use of MML refers to, for example, the technology assisting in arriving at the correct diagnosis for a particular patient. Clinical decision-making aids of MML refers to e.g. determining the clinical steps that need to be taken for an individual with a particular medical

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[16] Edward H Shortliffe and others, 'Computer-Based Consultations in Clinical Therapeutics: Explanation and Rule Acquisition Capabilities of the MYCIN System' (1975) 8 Computers and Biomedical Research 303.
[17] Edward H Shortliffe, 'Artificial Intelligence in Medicine: Weighing the Accomplishments, Hype, and Promise' (2019) 28 Yearbook of medical informatics 257.
[18] Shortliffe (n. 17).
[19] Nabile M Safdar, John D Banja and Carolyn C Meltzer, 'Ethical Considerations in Artificial Intelligence' (2020) 122 European Journal of Radiology 108768.
[20] Sudhen B Desai, Anuj Pareek and Matthew P Lungren, 'Current and emerging artificial intelligence applications for pediatric interventional radiology' (2021) Pediatr Radiol, https://doi.org/10.1007/s00247-021-05013-y.
[21] Shortliffe (n. 17). Emily Shearer, Mildred Cho and David Magnus, 'Chapter 23 - Regulatory, Social, Ethical, and Legal Issues of Artificial Intelligence in Medicine' in Lei Xing, Maryellen L Giger and James K Min (eds), *Artificial Intelligence in Medicine* (Academic Press 2021) 458.

condition, and its severity.[22] All of these applications are of importance to enhancing pediatric diagnostics, prognostics and care. In pediatric medicine, many MML applications have already been explored, including tools for prognosis, diagnosis, and therapy of pediatric critical care;[23] pediatric radiology;[24] airway management,[25] and pediatric severe sepsis prediction[26].

The development of MML technology is complex and requires accounting for a number of questions and challenges.[27] One of the central concerns is the availability of adequate training data.[28] The aim of selecting adequate data is to not only create software that functions for its given purpose in different environments, and strikes an appropriate balance between false positive and negative cases, but also to design it in a way that it is capable of dealing with potential bias[29] and that is able to address unanticipated patient contexts (known as out of sample input).[30] Admittedly, this is not a straightforward task.[31] Challenges such as these need to be tackled with due regard to the specificities of pediatric patients as a group and different subgroups therein. Generally, this patient group

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[22] Fei Jiang and others 'Artificial intelligence in healthcare: past, present and future' (2017) 2 Stroke and Vascular Neurology, doi: 10.1136/svn-2017-000101.

[23] Jon B Williams, Debjit Ghosh and Randall C Wetzel, 'Applying Machine Learning to Pediatric Critical Care Data*' (2018) 19 Pediatric Critical Care Medicine 599.

[24] Michael M Moore and others, 'Machine Learning Concepts, Concerns and Opportunities for a Pediatric Radiologist' (2019) 49 Pediatric Radiology 509.

[25] Clyde Matava and others, 'Artificial Intelligence, Machine Learning and the Pediatric Airway' (2020) 30 Pediatric Anesthesia 264.

[26] Sidney Le and others, 'Pediatric Severe Sepsis Prediction Using Machine Learning' (2019) 7 Frontiers in Pediatrics 413.

[27] For an overview see Robert Challen and others, 'Artificial Intelligence, Bias and Clinical Safety' (2019) 28 BMJ Quality & Safety 231.

[28] Challen and others (n. 27).

[29] Learned biases formed on human-related data frequently resemble human-like biases towards race, sex, religion, and many other common forms of discrimination. Daniel James Fuchs, 'The Dangers of Human-like Bias in Machine-Learning Algorithms' (2018) 2 Missouri S&T's Peer to Peer 1.

[30] Kun-Hsing Yu and Isaac S Kohane, 'Framing the Challenges of Artificial Intelligence in Medicine' (2019) 28 BMJ Quality & Safety 238. This, however, in itself might not be sufficient to deal with the possible disease pattern changes. Model updating protocols are suggested as means to tackle that challenge, see Sharon E Davis and others, 'Calibration Drift in Regression and Machine Learning Models for Acute Kidney Injury' (2017) 24 Journal of the American Medical Informatics Association 1052.

[31] Challen and others (n. 27).

is diverse and complex.[32] The different patient subgroups that the pediatric group captures have different biological preconditions that must be particularly considered when developing medical care, in addition to the disease or condition-specificities and other factors that could have an impact on the medical assessment and MLL device performance in pediatric care. The considerations, such as these, shape the data selection criteria (in addition to the common bias concerns, such as ethnicity, gender) for the development of the MML technology and fragment the landscape of available data.

3 General remarks on the EU regulatory approach

The EU seeks to become a global leader in health-related AI applications.[33] Thus, it comes as no surprise that within the EU following the aspiration set out in Article 179(1) TFEU to achieve a European research area and to encouraging it to become more competitive, considerable investments are made to realize the potential that AI and MML hold for healthcare. Already in the IMI2 programme within the framework of Horizon 2020[34] considerable focus was placed on the development of new digital health solutions. This emphasis continues under the current Horizon Europe programme.[35] In parallel, considerable policy and law-making work in the field has been done in order to tackle the chal-

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[32] See Kavot Zillén, Jameson Garland and Santa Slokenberga, 'The Rights of Children in Biomedicine: Challenges Posed by Scientific Advances and Uncertainties' (Council of Europe 2017).

[33] Bruno Catteneo, 'Being Smart about Our Health: How Artificial Intelligence Can Help Transform Europe's Health Sector' (*EU Science Hub - European Commission*, 3 February 2021) <https://ec.europa.eu/jrc/en/news/being-smart-about-our-health-how-artificial-intelligence-can-help-transform-europe-s-health-sector> accessed 6 September 2021.

[34] 'IMI Mission and Objectives' (*IMI Innovative Medicines Initiative*) <http://www.imi.europa.eu/about-imi/mission-objectives> accessed 4 October 2021. 'History – the IMI Story so Far' (*IMI Innovative Medicines Initiative*) <http://www.imi.europa.eu/about-imi/history-imi-story-so-far> accessed 4 October 2021.

[35] AI is one of the cornerstones of the EU Innovative Health Initiative (new proposed public-private partnership (PPP) under Horizon Europe), see The Innovative Health Initiative, 'Strategic Research and Innovation Agenda' <https://www.imi.europa.eu/sites/default/files/uploads/documents/About-IMI/IHI/IHI_SRIA_DraftJune2021.pdf> accessed 4 October 2021. 'EU to Set up New European Partnerships' (*European Commis-*

lenges and leash the potential that AI generally[36] and AI in the health field holds.[37]

Realizing this EU aspiration for a competitive position in health-related AI and simultaneously furthering the Member States' responsibility regarding children's health rights, that is, the right to health and the right to benefit of scientific advances, as formulated by the UN in the ICESCR, relates to several areas where the EU has legislative competencies. Neither of them is sufficient in themselves for realizing the potential that MML holds for pediatric medicine (i.e. lack of exclusive competence), and complementary actions on the part of the Member States might be needed. However, taken together, they capture key elements and consequently preempt the Member States from the action in the field. Thus, a careful navigation on the principle of conferral and the domain of shared and complementary competence and an investigation of how it has been exercised is necessary.

To begin with, the development of pediatric AI-based medical devices requires the availability of a sufficient amount of appropriate health data. As previously noted, the pediatric patient group is fragmented, and consequently so is the pediatric data landscape. The current central framework in that regard is the General Data Protection Regulation (GDPR).[38] It sets out rules to safeguard the rights of natural persons, whilst also ensuring free movement of personal data. In regard to scientific research, considerable discussions have emerged regarding the GDPR's potential negative impact, e.g. data sharing hurdles that are now attributable to the

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sion – European Commission) <https://ec.europa.eu/commission/presscorner/detail/en/ip_21_702> accessed 4 October 2021.

[36] See, for example, 'Expert Group on AI | Shaping Europe's Digital Future' <https://digital-strategy.ec.europa.eu/en/policies/expert-group-ai> accessed 7 October 2021.

[37] Recently, also the ethical and societal impacts of the AI in medicine and healthcare technology have been chartered to inform policy-making AI Watch Artificial Intelligence in Medicine and Healthcare: applications, availability and societal impact p. 13 European Commission. Joint Research Centre., *Artificial Intelligence in Medicine and Healthcare: Applications, Availability and Societal Impact.* (Publications Office 2020) 13 <https://data.europa.eu/doi/10.2760/047666> accessed 4 October 2021.

[38] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (Text with EEA relevance) OJ L 119, 4.5.2016, p. 1–88.

GDPR.[39] In response to the challenges in the field and in order to realize the potential that big data hold in the field of health and medical care, the European Health Data Space is under the development. The European Commission has committed to present its proposal in the last quarter of 2021,[40] thus at the moment of writing, it is uncertain whether and to what extent it could heal the existing challenges. Additionally, within the EU, stand-alone software for healthcare purposes could fall within the scope of a definition of a medical device provided in Article 2(1) of the Medical Devices Regulation (MDR).[41] Consequently, it shall comply with the detailed quality requirements prescribed by the regulation. Finally, the European Commission has put forward a proposal for regulating AI (proposed AIR).[42] Thus, in a near future, once the proposed AIR passes the legislative stage and enters into force also those requirements will need to be followed.

4 GDPR and development of pediatric AI tools

The development of AI/MLL medical devices intended for pediatric care is a data-intensive activity. There are a number of data sources that can cater to the need. For example, data may be obtained from research repositories, such as biobanks, or from the clinical or public health environment, for example, electronic health records or public insurance data. Data that may also be obtained non-clinically, for example, collected

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[39] See, for example, Santa Slokenberga, 'Setting the Foundations: Individual Rights, Public Interest, Scientific Research and Biobanking' in Santa Slokenberga, Olga Tzortzatou and Jane Reichel (eds), *GDPR and Biobanking: Individual Rights, Public Interest and Research Regulation across Europe* (Springer International Publishing 2021).

[40] Vincent Draguet, 'European Health Data Space' (*Public Health - European Commission*, 18 September 2020) <https://ec.europa.eu/health/ehealth/dataspace_en> accessed 4 October 2021.

[41] Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance) OJ L 117, 5.5.2017, p. 1–175. See Article 2(1) for the definition.

[42] Proposal for a Regulation of the European Parliament and of the Council Laying Down Harmonised Rules on Artificial Intelligence (Artificial Intelligence Act) and Amending Certain Union Legislative Acts COM/2021/206 final.

from wearables or mobile devices and be used in the development of MML devices.[43]

The General Data Protection Regulation (GDPR) could be said to have a rather complex relationship with the development of pediatric MML tools. Generally, the GDPR per se is not a research regulatory instrument.[44] However, it contains a research regime and prescribes particular rules that shall be followed when personal data are processed. The development of MML devices for pediatric care in the EU commonly will risk triggering the application of the GDPR, except for when anonymized data are used for the purpose.[45] While there could be parts of a study that could be performed, using anonymized data and thus it would not trigger the application of the GDPR, there will be MML research that is difficult to perform anonymously, in either full or in part. Moreover, even if anonymity might seem an option, the degree of anonymity could be an illusion.[46] In cases such as those, the application of the GDPR is rather unavoidable.[47]

The GDPR does not further any particular type of scientific research in a direct way. However, at the same time, the development of pediatric MML devices falls under the broader spectrum of public interest in the area of public health.[48] The domain of public interest, both separately and within the area of scientific research, can be subject to further particularly lax requirements.[49] Thus, although the development of pediatric MML devices is located within the general research regime, it has potential to benefit from the specific public interest rules.

In order for the development of a pediatric AI tool to take place, the particular data processing activities underlying its development needs to be regarded as lawful within the meaning of the GDPR. This entails meeting the general requirement for a lawful basis for personal data processing under Article 6(1) as well as the specific requirement in relation to sensitive personal data, which includes health data, under Article 9(2). Article 6(1) does not treat scientific research in any special way and thus,

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[43] Shearer, Cho and Magnus (n. 21) 459.

[44] Slokenberga, 'Setting the Foundations' (n. 39) 17.

[45] See Recital 26 and Article 2(1) GDPR.

[46] Paul Ohm, 'Broken Promises of Privacy: Responding to the Surprising Failure of Anonymization' (2009) 57 Ucla L. Rev. 1701.

[47] See Article 2(1) GDPR.

[48] Recital 159 GDPR.

[49] See Slokenberga, 'Setting the Foundations' (n. 39) 11–27.

the research activity needs to meet one of the general legal grounds, such as consent or public interest, set forth in that provision. Article 9(2), however, does treat scientific research specifically in Article 9(2)j, where processing that is necessary for scientific research purposes is explicitly mentioned as one of the exceptions to the general prohibition (Article 9(1)) to process sensitive data This does not mean that other legal grounds are irrelevant, especially, if the freedom that is afforded to the Member States under Article 9(4) GDPR is accounted for. This provision *expressis verbis* allows the Member States to maintain or introduce further conditions, including limitations, with regard to the processing of genetic data, biometric data or data concerning health. These further regulations could theoretically be such that they treat pediatric AI research in a special way if this treatment is shaped in line with the general principles of EU law. However, a study carried out by the EU does not show that thus far it has been used for that purpose.[50]

While the GDPR prescribes several alternative legal grounds that could be used for the processing of personal data in developing MML devices for pediatric patients, not all of them might be equally suitable or desirable for the purpose. Generally, in the field of scientific research, and in particular, in the aftermath of the WWII, the principle of informed consent has been of paramount importance. While, as explicitly illustrated by the GDPR rules, data-driven research has drifted from that approach, informed consent is still commonly recognized as a safeguard in processing personal data for research purposes, disregarding whether it is used as legal basis for data processing.[51] The GDPR enables several alternative legal basis for the processing of personal data, however, preference of another legal basis over consent could be regarded as sensitive and in conflict with the sense of ownership that people could have about their data, even if this sense of ownership is rather illusory.[52] The tensions that using other legal basis instead of consent is in conflict with the sense of ownership people could have regarding their data (or responsibility for

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[50] DG Health and Food Safety, 'Assessment of the EU Member States' Rules on Health Data in the Light of GDPR' (European Union 2021).

[51] GDPR (n. 38) recital 33. See also Ciara Staunton, Santa Slokenberga and Deborah Mascalzoni, 'The GDPR and the Research Exemption: Considerations on the Necessary Safeguards for Research Biobanks' (2019) 27 European Journal of Human Genetics 1159.

[52] Santa Slokenberga, 'You Can't Put the Genie Back in the Bottle : On the Legal and Conceptual Understanding of Genetic Privacy in the Era of Personal Data Protection in Europe' [2021] Biolaw Journal - Rivista di Biodiritto 223.

their child's data), and could be illustrated by such case as the Italy – IBM Watson Health case and Google Health – NHS case, even though both occurred pre-GDPR application period and one can question how these cases would evolve had they occurred under the GDPR. Regarding the former, it has been reported that detailed medical records of 61 million Italian citizens have been provided to IBM Watson Health by the Italian government.[53] Among the concerns that have been highlighted is lack of consent of the persons concerned.[54] While the data scale was different in the Google Health – NHS case, also this transfer brought along considerable questions regarding the collaboration, and lack of the data subjects' control over the transfer through their consent.[55]

Further to the legal basis through which the development of MML for pediatric care could be furthered, also other research-furthering legal interventions are possible under the GDPR. One such is the derogation from individual rights that the GDPR provides for the data subjects in Chapter III. The extent of derogations will depend on a particular activity and circumstances surrounding the research. However, more generally it could be said that the GDPR enables a two-level derogation avenue.[56] First, through the direct application of the individual rights provisions that permit derogations through Article 89(1) GDPR, and secondly, through national law or EU law that prescribes particular derogations in accordance with Article 89(2) GDPR. While Article 89(2) in itself does not explicitly enable the Member States or the EU to treat a particular research field specifically, it could be done considering the discretion that the Member States have under Article 9(4) GDPR, and in so far as it is exercised in line with the fundamental principles of EU law. More-

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[53] 'Detailed Medical Records of 61 Million Italian Citizens to Be given to IBM for Its "Cognitive Computing" System Watson' (*PIA VPN Blog*, 22 May 2017) <https://www.privateinternetaccess.com/blog/detailed-medical-records-61-million-italian-citizens-given-ibm-cognitive-computing-system-watson/> accessed 4 October 2021.

[54] Janos Meszaros, Marcelo Corrales Compagnucci and Timo Minssen, 'The Interaction of the Medical Device Regulation and the GDPR: Do European Rules on Privacy and Scientific Research Impair the Safety & Performance of AI Medical Devices?' in Glenn I Cohen and others (eds), *The Future of Medical Device Regulation: Innovation and Protection* (Cambridge University Press (available at Social Science Research Network) 2021) <https://papers.ssrn.com/abstract=3808384> accessed 4 October 2021.

[55] Julia Powles and Hal Hodson, 'Google DeepMind and Healthcare in an Age of Algorithms' (2017) 7 Health and Technology 351.

[56] Considering Article 23 GDPR derogations, a three-level avenue. Slokenberga, 'Setting the Foundations' (n. 39).

over, this freedom would also need to be considered accounting for other circumstances, for example, Member State's international commitments and research regulatory traditions.

MML for pediatric care and public interest concept adds further nuance and possibilities to further scientific research and development of technology for this patient group.[57] To begin with, already recital 159 GDPR indicates that research that is carried out in the field of public health is in the public interest. As such, it could benefit from a particular legal basis under Article 9(2) GDPR as well as other specific derogations that are prescribed in the GDPR. At the extreme, if the degree of public interest reaches the level of an "important objective of general public interest", Article 23(1)(e) GDPR could be triggered, which enables far-reaching derogations from the GDPR rules. There are, however, several challenges with the application of the public interest rule under the GDPR. For example, there is a lack of detailed guidance on the concept of public interest as well as on the threshold to measure and classify the level of interest.[58] It is thus uncertain not only what level of public interest MML in pediatric medicine could trigger, but also whether all MML in the field should be treated the same way, or pediatric MML, given the challenges in pediatric medicine generally, could be subjected to particular rules.[59]

5   AI in pediatric care and development of medical devices

The Medical Devices Regulation (MDR) subjects any software intended for the prediction or prognosis of a disease or monitoring of treatment,[60] to its requirements. Substantively, the regulation sets forth rules concerning the placing on the market, making available on the market or putting into service of MML pediatric devices.[61] The EU does not claim any general competence over the regulation of the clinical investigation of med-

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[57] However, as elsewhere has been noted, what public interest is not something that is well-elaborated within the GDPR, see Slokenberga, 'Setting the Foundations' (n. 39).
[58] Recital 73 affirms the wording of Article 23(1)(e) GDPR.
[59] Meszaros, Corrales Compagnucci and Minssen (n. 54) 3.
[60] MDR (n. 41) article (1).
[61] MDR (n. 41) article 1(1).

ical devices.[62] However, where a clinical investigation is carried out as part of the clinical evaluation for conformity assessment purposes it shall meet the requirements prescribed by the regulation.[63] This could be said to be a rather technical regulatory approach to hide a larger pre-empting policy behind the EU's teeth, as any software placed on the market, made available on the market or put into service within the EU shall meet the requirements set out in the regulation.[64] Thus, a medical device that does not meet the prescribed requirements cannot be made available to the users.[65]

As a starting point, a pediatric MML device shall meet the applicable general safety and performance requirements.[66] Identification of the relevant general safety and performance requirements that a particular MML pediatric device shall meet under the MDR lies with the manufacturer. Moreover, manufacturers shall also specify and justify the level of clinical evidence that is necessary in order to verify whether they are met.[67] Generally, any medical device shall be suitable for the intended purpose. Moreover, the device shall be safe and effective and shall not compromise the clinical condition or the safety of patients, healthcare personnel or other persons. While the general requirements aspire to ensure a high level of protection of health and safety, they also acknowledge that some risks could be deemed acceptable when weighed against the benefits to the patient.[68]

In addition to the general safety and performance requirements, other requirements also apply, given the nature of a particular medical device. While the regulation does not prescribe any particular requirements re-

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[62] It is defined as "any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device", MDR (n. 41) article 2(45).
[63] MDR (n. 41) article 62(1).
[64] The application of the clinical investigation requirements is subjected to meeting at least one of the further in the regulation specified applicability requirements in article 62(1) of the Regulation. Those are as follows: either 1) to establish and verify that the device in question achieves the performance intended as specified by its manufacturer, or 2) to establish and verify the clinical benefits of a device as specified by its manufacturer, or 3) to establish and verify the clinical safety of the device and to determine any undesirable side-effects, and assess whether they constitute acceptable risks when weighed against the benefits to be achieved by the device.
[65] See MDR (n. 41) article 5.
[66] MDR (n. 41) article 5(2).
[67] MDR (n. 41) article 61(1). For the requirements see annex I.
[68] See MDR (n. 41) annex I.

garding medical devices containing a ML component specifically or AI component generally, it sets relevant requirements that are applicable to any software. Thus, for example, software, such as pediatric MML, shall be designed to ensure repeatability, reliability and performance in line with their intended use. Moreover, it shall be developed and manufactured in accordance with the state of the art considering the principles of the development life cycle, risk management, including information security, verification and validation. The manufacturer shall also determine minimum requirements concerning hardware, IT networks characteristics and IT security measures. Finally, when software is intended to be used in combination with mobile computing platforms, compatibility requirements e.g. size and a contrast ration of a screen, as well as different environments need to be accounted for.[69]

The verification procedure of the requirements that MML pediatric devices will need to meet under the MDR depends on the classification of a particular device. The higher the risks associated with a particular device vis-à-vis the human body,[70] the higher the classification it has. The regulation does not prescribe any particular requirements for the MML devices intended for pediatric patients. The general requirements apply. As derives from Rule 11 of Annex VIII of the Regulation, any software that does not fall within a particular exception specified within this rule shall be classified as a class I device.[71] Exceptions are as follows. Software that is intended to provide information that is used to make decisions with diagnosis or therapeutic purposes is classified as class IIa device. However, if such decisions have an impact that may cause death or an irreversible deterioration of a person's state of health, then the device shall be classified as a class III device. In case such decisions have an impact that may cause serious deterioration of a person's state of health or surgical intervention, then the device shall be classified as a class IIb device. Generally, software that is intended to monitor physiological processes is classified as class IIa; however, if it is intended for monitoring of vital physiological parameters, where the nature of variations of those parameters is such that it could result in immediate danger to the patient, it is classified as class IIb.

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[69] MDR (n. 41) annex I, chapter II, section 17.
[70] See MDR (n. 41) recital 58. See also annex VIII, chapter II, section 3.1.
[71] See MDR (n. 41) article 51 and annex VII, rule 11.

The classification particularly relates to different procedures for the conformity assessment of the devices, and the degree of involvement of the notified body in the assessment.[72] Class I devices are associated with a low level of vulnerability. Hence, the conformity assessment procedure should be carried out under the sole responsibility of manufacturers.[73] For class IIa, IIb and class III devices, a particular level of involvement of a notified body is mandated.[74] The involvement of a notified body seeks to ensure that it has assessed the conformity to the applicable requirements under the MDR; however, the modalities of the involvement differ for different device classes and the MDR leaves some room for choice regarding the exact procedure that is to be followed.[75] One of the key implications of a particular MML pediatric device falling beyond class I is that it will be subject to a conformity assessment carried out by a notified body. A successful assessment procedure results in a conformity assessment certificate,[76] attachment of a CE mark indicating that the applicable requirements of the MDR are met.[77]

The degree of involvement of a notified body in the conformity assessment procedure for class IIa, IIb and III devices depends on the modalities of the conformity assessment and particular audit requirements. One central aspect in all assessments that are based on a quality management system and assessment of technical documentation is audit.[78] For MML pediatric medical devices, this could include reviewing of input data that are laying at the core of the devices. This raises such questions as the existence of appropriate expertise of the notified bodies for carrying out such a review.[79] In addition to the necessary knowledge regarding a particular medical application and condition in question, also particular understanding of the pediatric patient group is necessary, along with an understanding of the risks of bias in the respective group. Moreover, the standard will be regarded as adequate in order to be considered as meet-

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[72] Choice of a notified body is addressed in article 42.

[73] MDR (n. 41) recital 60.

[74] MDR (n. 41) recital 60.

[75] See MDR (n. 41) article 52 that sets out general rules on conformity assessment procedure.

[76] MDR (n. 41) article 56.

[77] MDR (n. 41) article 20.

[78] See MDR (n. 41) annex IX.

[79] Meszaros, Corrales Compagnucci and Minssen (n. 54) 3.

ing the applicable requirements is also uncertain, and how it will differ between different purposes in pediatric medicine.

6   How, if at all, the proposed AI Regulation change the landscape?

Different MML approaches, including supervised, unsupervised and re-inforcement learning, using a wide variety of methods including deep learning, fall within the scope of the application of the proposed AI Regulation (AIR) as AI-systems.[80] Thus, any pediatric MML device is also expected to trigger the application of the proposed AIR once it is passed and enters into effect.

The proposed AIR neither enables nor facilitates a particular field of AI application. It is a standard setter; and as such, it sets uniform principles in the attempt to ensure safe and reliable AI systems within the EU.[81] In that regard, it creates a three-level risk regime. The AI systems that create an unacceptable level of risk are prohibited. The AI systems that pose a high-risk fall within a particular high-risk regime set forth within the proposed AIR. The devices that fall within the low or minimal risk regime fall under the general requirements prescribed within the proposed AIR. The high-risk AI system regime captures those AI-systems that are of importance for the functioning of the society, as well as individuals, such as medical devices.[82] This means that they are subjected to strengthened legal requirements, including regarding accuracy, robustness and cybersecurity,[83] and the requirement if a human oversight.[84]

As a general rule, any high risk devices, including pediatric MML devices may only be placed on the market or put into service if the requirements

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[80] Proposal for a Regulation of the European Parliament and of the Council Laying Down Harmonised Rules on Artificial Intelligence (Artificial Intelligence Act) and Amending Certain Union Legislative Acts COM/2021/206 final, annex III.

[81] See proposed AIR (n. 80) recital 18 and article 1.

[82] See proposed AIR (n. 80) article 6 in conjunction with annex II.

[83] Proposed AIR (n. 80) article 15.

[84] Proposed AIR (n. 80) article 14.

that the proposed AIR prescribes are met.[85] As previously noted, adequate data is an essential precondition in developing MML pediatric devices. The proposed AIR sets forth requirements for the training, validation and testing data sets that are used in the development of pediatric MML medical devices as high-risk AI systems. It requires that these data sets be subject to "appropriate data governance and management practices".[86] The appropriateness is intended to include availability, quantity, as well as suitability of the data sets for the intended products.[87] The proposed AIR sets forth further requirements for the data used in developing pediatric MML medical devices. This means that the data sets that are used in the development of a device shall be relevant, representative, free of errors and complete, including with due regard to the specificities of a particular user group.[88] Moreover, these data sets shall also account for the characteristics or elements that are particular to the specific setting within which the pediatric medical device is intended to be used.[89] Thus, although the proposed AIR sets forth a framework that aim to ensure that adequate data sets are used for developing pediatric MML medical devices, what adequate is will need to be assessed based on the state of the art, as well as a particular case at hand. As the responsibility lies with the manufacturer, divergences in the approaches for managing data can be foreseen that can reflect in the technicalities and the performance of the device.

Similarly as for medical devices generally, also for AI-systems a technical documentation needs to be drawn up before a particular system is placed on the market or put into service.[90] For medical devices specif-

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[85] Proposed AIR (n. 80) article 19.1. Central requirements: an iterative risk management system needs to be established, implemented and documented (article 9). In the development, datasets that meet prescribed governance and management requirements shall be used (article 10). The high-risk AI system shall have automatic recording capacity while the system is operating (article 12). It shall be designed and developed in such a way to ensure that their operation is sufficiently transparent for the users (article 13) and that they can be effectively overseen by natural persons when in use (article 14). Moreover, they shall achieve an appropriate level of accuracy, robustness and cybersecurity, and maintain this throughout their lifecycle (article 15) Finally, adequate technical documentation needs to be drafted that allows assessing compliance with the applicable requirements set out in the proposed AIR (article 11).

[86] Proposed AIR (n. 80) article 10(6).

[87] See Proposed AIR (n. 80) article 10; in particular, 10(2)(e).

[88] Proposed AIR (n. 80) article 10(3).

[89] Proposed AIR (n. 80) article 10(4).

[90] Proposed AIR (n. 80) article 18(1).

ically, one single document needs to be drawn that contains both, the information mandated under the MDR, as well as information necessary under the proposed AIR.[91] An overarching requirement is set forth, that this documentation needs to be "kept up to date" and is drafted in a way that enables ascertaining compliance with the applicable requirements set out in the proposed AIR.[92] While the minimum requirements are outlined in the proposed AIR, further requirements could apply due to the nature of the device in question. Moreover, in light of the technical progress, the European Commission has been delegated the power to specify other requirements through relevant amendments in the proposed AIR annex IV.[93]

An essential element prior to placing on the market or putting into service high risk pediatric devices is conformity assessment, an obligation that generally lies with the providers (developers) of the devices.[94] However, exceptionally, for health purposes derogation of this requirement could be possible.[95] This assessment is based on the quality management system assessment of technical documentation, including granting of the availability for the examination of the datasets used for developing the device.[96] In examining the technical documentation, the notified body is enabled to require that the provider supplies further evidence or carries out further tests to enable a proper assessment of conformity of the AI system with the applicable requirements. However, if the notified body is not satisfied with the tests carried out by the provider, the notified body shall directly carry out adequate tests, as appropriate.[97] This mean that at this stage, the notified body is entrusted with a far-reaching obligation in carrying out the assessment.

For the users, of central importance is Article 13 that sets forth transparency and provision of information requirements. It is required that AI systems are designed and developed in a way that allows ensuring that their operation is sufficiently transparent to enable the users of a device to interpret the system's output and use it appropriately.[98] Moreover, this

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[91] Proposed AIR (n. 80) article 11(2).

[92] Proposed AIR (n. 80) article 11(1).

[93] Proposed AIR (n. 80) article 11(3). See article 3(1 *sic*) for the definition of a provider.

[94] See Proposed AIR (n. 80) article 19(1) and 43.

[95] Proposed AIR (n. 80) article 47.

[96] Proposed AIR (n. 80) annex VII, section 4.3.

[97] Proposed AIR (n. 80).

[98] Proposed AIR (n. 80) article 13(1).

information shall meet certain quality requirements, including regarding conciseness, completes, correctness and clarity, and be relevant, accessible and comprehensible to the intended users of the device.[99] The regulation sets forth further modalities of the information,[100] including particular requirements relevant for enabling the user to understand the performance of the device. One of the challenges in pediatric care will relate to ensuring that appropriate information is provided to the patients as users of the devices, given the peculiarities of different patient groups.

7   Concluding reflections

As becomes rather apparent, none of the three legal instruments is concerned with directly furthering the development of the pediatric MML devices. What concerns the GDPR, it can be noted that a number of mechanisms are inbuilt within the framework that enable and could even further data processing. However, a closer look at the legal basis system reveals a different image. While the GDPR sets forth various legal basis for personal data processing, it does not address preconditions for accessing these data. The Member States retain freedom to decide who and under what circumstances are able to access data for research purposes. Consequently, in itself, it is insufficient for furthering scientific research. For example, the GDPR in itself cannot be used as basis to claim access to the patient data from the national electronic health records for scientific research purposes in order that the development of pediatric MML can take place. This could, however, happen if there is, for example, appropriate national law in place securing the access.[101] This could be said to be one of the central shortcomings in developing pediatric MML, as often-multinational collaboration will be necessary to cater for the data need for a particular patient group. More broadly, it could be argued to be also one of shortcomings of the GDPR research regime generally, and something that should be carefully considered as the European Health Data Space is being developed.

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[99] Proposed AIR (n. 80) article 13(2).

[100] Proposed AIR (n. 80) article 13(3).

[101] This anchors in an argument that access rights and the control over personal data shall not be reduced to the legal basis for the processing of personal data, and fulfilling respective processing preconditions.

The MDR provides a rather principle-based framework to further a high level of health and safety requirements for the MML pediatric devices. For the devices that require the involvement of the notified body, it designs a balanced mechanism whereby the manufacturer decides on the applicable requirements and ensures that they are met, whereas the notified body verifies whether the requirements are met. Whether this approach is adequate for ensuring qualitative pediatric MML devices remains to be seen. As usual, the devil is in the details, and in particular the assessment of how the applicable principles set out in the MDR play out in an individual MML pediatric device case.

The proposed AIR, the newcomer in the regulatory spectrum, generates rather complementary effects with the MDR. In particular, in regard to the applicable requirements for the performance of software as a medical device. It should then be so that data quality requirements set out in the proposed AIR are relevant for meeting the standard that the MDR requires. The synergy between two instruments is through, for example, the single technical documentation requirement, which needs to be drafted in a way to meet the requirements of both of the applicable instruments, as well as the conformity assessment mechanisms.[102] Ultimately, at least on the surface, the two instruments should generate a mechanism for ensuring qualitative pediatric MML devices in the internal market.

While the EU has preempted Member States form action in the area of pediatric MML devices to a considerable degree, in particular, regarding conditions for data processing, as well as quality requirements for medical devices and AI-systems, these mechanisms fail to generate concrete initiatives for development of these devices, and thus enhancing availability of medical care. Only the GDPR contains a mechanism that could further the development, albeit in a rather indirect way. This is in contrast with the long-existing mechanism to further the development of pediatric medical products through an internal market regulation,[103] and could risk leading to a situation where a particularly marginalized patient group is also down-prioritized in the development of new pediatric MML devices.

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[102] Proposed AIR (n. 80) article 43(3).
[103] Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (Text with EEA relevance) OJ L 378, 27.12.2006, p. 1–19.