

Invited Paper

“High-risk for cerebral palsy” designation: A clinical consensus statement

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1. Introduction

According to UNICEF, 2.35 billion children across the world were under the age of 18 in 2020 [1]. Of these children, between 4.7 and 8.7 million currently have cerebral palsy (CP), as determined using prevalence rates for developed versus low-income and developing countries [2–5, 6]. From a slightly different perspective, every year 350,000 to 500,000 newborn infants worldwide are likely to receive a CP diagnosis during their lifetime. Without a change in our current clinical diagnostic process, the families of these children will continue their disempowered waiting, children will miss out on opportunities for targeted interventions during a critical period of neuroplastic change, and our policies will continue to support delayed diagnosis and intervention.

This consensus statement stemmed from the concerns of a large Implementation Network of providers

across North America and colleagues abroad. The authors of this consensus statement represent primarily clinical providers in multiple disciplines, some researchers who focus on CP diagnosis and treatment, and policymakers who support the need for change. A brief history, rationale, parent perspectives on the proposed designation, as well as future directions are contextually provided after the statement.

2. Consensus statement from the Implementation Network for Early CP Detection and Intervention [7]

Given the need to balance the access to or imprecision of certain elements of early detection, the complexities of multiple healthcare systems and the lack of direct and specific guidance from governing bodies in clinical and academic medicine, it falls to clinicians, implementers and researchers to work together to find common ground to serve the best interests of patients. A recent article on ethical issues in CP [8] inspired a framework that our Implementa-

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tion Network used to find a solution to the conundrum of early diagnosis during early CP detection.

We have decided to adopt a "High-Risk for CP" designation as early as possible when infants are under the age of 2 years. The purpose of this clinical designation (as opposed to ones used for research, systematic reviews or other types of scientific publications) is primarily to use a common language and to start joint decision-making and goal-setting conversations with parents. The purpose is never to delay giving an early diagnosis.

1. By adopting a clearly defined designation of "High-Risk for CP," we can be transparent with parents surrounding our concerns (respect for person). In this manner, we both acknowledge the autonomy of the parent as an individual deserving of truth, information and education as well as acknowledging the need to protect vulnerable infants whose diminished autonomy makes them reliant on an informed caregiver. A high-risk designation then ensures early education and empowers autonomy of our families and patients.
2. By adopting a clinically meaningful designation of "High-Risk for CP," we abide by the principle of beneficence in clinical care: we ensure that parents and children are treated in an ethical manner by making efforts to secure their well-being through early, justified referrals for family supports and therapeutic or diagnostic services for patients. Failing to examine the hypothesis suggested by compelling basic science data that an optimal window of opportunity for restoration may be possible in human infants also poses an ethical challenge.
3. Finally, by giving a designation of "High-Risk for CP" in a systematic and understandable manner, while acknowledging the limits of our knowledge as practitioners, we ensure access to information (or education) and services for all, regardless of individual or systems challenges (e.g., personal discomfort with difficult diagnoses and uncertainty, persistent professional practices of delaying CP diagnosis until after the age of 2 years, intrinsic or extrinsic biases). Equitable support of families through a standardized approach to designation, using appropriate communication approaches (e.g., language, cultural awareness, assistive tools) and offering early parental supports, all reduce health inequities and disparities in CP, enabling

clinicians to abide by justice in care provision.

As such, we use the designation term "High-Risk for CP" when at the time of evaluation:

1. Either because an assessment was not performed or had a negative result, patients lack one of the essential components of the diagnosis of CP but have many others. Basic components include combinations of all of the following: clinical history consistent with etiology of CP (birth history or hospital stay), neurological exam with qualitatively documented impairments, quantitative decreases in motor function on standardized assessments, and biomarkers (genetic test positive for conditions associated with CP and not progressive disorders, Hammersmith Infant Neurological Exam (HINE) scores below threshold for age as documented in the most current review [9] or general movements pattern falling into cramped synchronized or absent fidgety categories), OR
2. Alternatively, when the clinician is evaluating the child for the first time well before the age of 2 years and no previous evaluations have demonstrated clear concerns. In this case, the designation acknowledges the value of repeated measurements of certain assessments (neurological exams, motor function evaluations) as they can change rapidly through the first two years due to developmental timing in specific populations (e.g., prematurity, prolonged hospitalization and ventilation, intrauterine drug exposures). It also acknowledges the imprecision inherent in using tests of motor function performed to assess capacity or patterns (vs. performance) in establishing the motor impairment that defines CP.

3. CP as a heterogeneous disorder

The term cerebral paralysis was used over 150 years ago to characterize individuals with longstanding contractures resulting from spasticity and weakness linked to brain injuries in infancy [10]. Since then, the definitions of CP have evolved to the most accepted one currently: "A group of disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorder

ders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behaviour, and/or by a seizure disorder." [11] Recently, the term "cerebral palsy spectrum disorders" has been proposed to acknowledge the complexity of etiologies and presentations of this group of developmental disorders, retaining the characteristic "early onset neuromotor impairment that can be attributed to a pathologically nonprogressive brain lesion" [12]. However, as in autism spectrum disorders (ASD) [13, 14], a spectrum of phenotypes, an "array of possibilities, exist in terms of the individual experience". Similarly, our knowledge of presentations linked to genetic etiologies has increased over time [15], and a larger portion of the spectrum of CP is now recognized as having a basis in uni- or multi-factorial genetic factors or causes [16, 17].

However, regardless of etiologies and presentations, clinicians, researchers, parents, and community stakeholders agree that the lifetime burden of CP is considerable. Few recent original research studies have explored economic costs, with a 2018 systematic review estimating that medical costs per child with CP were 10–26 times higher than for a child without visible disabilities [18, 19]. Morbidity across multiple domains is well documented [20, 21], and mortality increases for all, especially for those with more severe presentations [22]. The consequences of CP-related impairments in older adults are not yet fully understood as more adults adapt and face the consequences of an aging body and brain interacting with a disorder they may have previously accommodated. Research suggests long-term psychosocial impact of the diagnosis in adults, effects on employment opportunities, insurance and participation [23–26].

To continue a comparison with another developmental disorder, challenges in early ASD diagnosis persist but are the focus of extensive research and advocacy, efforts yet to be replicated for CP; these differences are not explained by simple statistics of disorder frequency: for example, funding allocated in the Centers for Disease Control's 2020 budget for ASD was \$23 million vs. \$2 million for Fragile X vs. \$0.0 (zero) for CP and can be contrasted for discrepancy with their respective prevalence in the US (1:44 vs. 1:10,000 vs. 1:345) [2, 27–29]. While the importance of ASD early diagnosis remains a priority for clinicians promoting early interventions [30], this has not been consistently the case for CP. Clinicians acknowledge that environmental, genetic, and age-dependent manifestations of a developmental disorder can result

in variable presentations [14, 31]. This can create a reluctance to diagnose before the developmental course of the disorder is established, often well into the third to fifth year after birth. Adding to the concerns, it was hypothesized that "outgrowing" CP was possible, although this has now been largely refuted [32, 33]. Clinicians then face the possibility that they either misdiagnosed or gave a diagnosis that may be expressed variably throughout their lifetime. Concerns in giving the diagnosis also range from those of potentially causing unnecessary distress to parents, labeling a child with potential social or economic consequences, or even preventing the investigation of a serious progressive or malignant condition [34, 35]. Recently, however, many concerns were alleviated through research in predictive and diagnostic tools, ability to understand functional and developmental changes over time, and to promote direct engagement of parents in feedback and goals [36].

4. Accurate and early detection tools and processes

In the past ten years, researchers have refined existing tools that help detect CP in the first years and predict likelihood, type, and severity of later CP [36–39]. Many of these tools have research strength to support them but as discussed later, the drawback of being developed through classical research studies. Some of the tools used for early detection remain the same as those traditionally used by clinicians in practice: a *clinical history* consistent with brain insults in the perinatal period, a *neurological exam* demonstrating impairments in infancy, and *tests of motor function* demonstrating delays and impairments. Tools emphasized in the first year now also include those with large scale and peer-reviewed published data, most with new systematic reviews and meta-analyses. These include but are not limited to (1) neuroimaging, both serial cranial ultrasounds and MRI with specific patterns predictive of CP [40–43]; (2) Prechtl's General Movements Assessment (GMA) with cramped synchronized or absent fidgety patterns [39]; and (3) the Hammersmith Infant Neurological Examination with scores below predicted threshold specific to defined age strata [9, 44].

With these new tools in hand, the Cerebral Palsy Alliance in Australia convened the International Multidisciplinary Prevention and Cure Team (IMPACT) for CP in 2014 [45] to develop an international consensus surrounding early detection and intervention

for CP [36]. This multidisciplinary group of clinicians, scientists, community stakeholders, individuals with CP, and parents reviewed and discussed the evidence through systematic reviews and focus groups. Their work resulted in a consensus manuscript with not only tools for early detection but, importantly, for implementation and pathways for those with identifiable risks in the newborn period and for those with risks identified after five months by caregivers or health care providers. This consensus statement recommended the use of a "high-risk CP clinical diagnosis" when "a diagnosis is suspected but cannot be made with certainty". The consensus manuscript faced difficulties in getting published, perhaps in part due to conceptual novelty of early diagnosis of CP.

In the intervening three years between the initial manuscript draft submission and the final publication in the summer of 2017, a U.S. team, who participated in IMPACT for CP, first implemented individual components of the guidelines (assessments) [46], followed by the full set of guidelines in 2016 [47]. Using implementation and educational science metrics, these teams demonstrated that (1) rigorous training could reliably result in standardized administration of clinical assessments; (2) 3–4 month clinic visits with elements of detection were feasible and sustainable; and (3) the average age at diagnosis could be lowered under 12 months of age with processes integrated into current healthcare systems. This early success led to a partnership with the U.S.-based Cerebral Palsy Foundation (CPF), whose main focus are community engagement, knowledge translation, and dissemination [48]. They were interested in funding implementation science projects and especially in the creation of a large network to scale up the work that started regionally [49].

Faced with increasing demand for education on the processes underlying guideline implementation for early detection of CP, the CPF and academic partners developed the first conference centered entirely on implementation of early detection and intervention for CP [50]. The innovative model for the conference was approved by the American Board of Pediatrics as providing a new model for interdisciplinary, workshop- and deliverable-based learning as well as more conventional educational opportunities. The conference and implementation processes developed from 2016 to 2019 have trained over 3,000 clinical practitioners throughout the U.S. and the world to date. In the meantime, other organizations also followed suit with Australia and others

implementing their own versions of early detection conferences and studies [51, 52].

5. Old and new concerns surrounding early detection

Though early detection has shifted on the curve of diffusion of innovation from innovators to early adopters, the tipping point has not yet been reached. Many of the challenges previously cited were reiterated along with some new and fact-based concerns [53, 54]. From a historical perspective on the elements of early diagnosis of CP, the state of early detection in the mid 2010s, and some of the central questions and challenges to early diagnosis, there is no better synopsis than the article by Dr. te Velde and colleagues, most of them the architects and innovators behind the guideline articles [55].

Some clinicians were still concerned about the impact of early diagnosis on parent wellbeing. These were addressed by a series of publications showing that parents wanted diagnoses as early as possible so they could obtain the education and start the advocacy process for their child as soon as possible. Parents had a positive perception of early diagnosis of CP [56]. Conversely, they felt resentment, anger, and mistrust when they felt medical providers were too vague with them or advocated a delayed approach to diagnosis [57]. Negative parent perceptions of providers who did not disclose potential CP diagnoses were, in turn, associated with worse mental health outcomes for parent and child in the long term. The impact of mistrust of the medical system can only be surmised from historical precedent in other medical domains, but it has been shown to impact access to care and long-term health outcomes [58]. In the current medical era, respect for parents as autonomous agents with the right to make informed decisions about their child's care is the expected standard with full and transparent access to their child's medical information [59]. Shared decision-making processes for complex patients are emerging areas of education, research, and implementation that will likely help allay some of the fears of causing psychological harm from early CP diagnoses [60, 61]. Finally, a very real concern existed that labeling a child with a diagnosis might cause long-term health care disparities (despite public stances and legal rights) due to conscious or unconscious biases, potential problems obtaining insurance coverage, and even employment when CP is disclosed.

Concerns also exist regarding the difficulty of guideline implementation for early detection due to access limitations for certain of the key detection elements. The first of the barriers is lack of educational opportunities. Prior to the development of workshops and standardized training, education in rigorous administration of the HINE was challenging. New training and train-the-trainer programs approved by the developers of the HINE, as well as large scale training and dissemination at professional conferences, has helped alleviate this concern. Access to Prechtl's GMA remains somewhat problematic, with few trainers across the world and a large upfront investment of time and resources on the part of individuals who wish to be trained [62]. In addition, while the rigor of the certification process ensures high fidelity and quality of results, maintaining this level requires frequent practice and occasional recalibration [63]. Prechtl's trust has made significant steps in ensuring improved access, with new trainers allowed to practice independently and more frequent lower-income country sponsored-training, as well as a consideration of new training models [62].

An often-overlooked obstacle to GMA implementation is the protection of patient health information privacy [64]. Recording the GMA requires the use of devices and information clouds managed by local hospital systems to ensure the highest levels of protection of identifiable patient video data. This process may be either unavailable or costly and not compatible with some phone-based applications. In the same category of resource barriers to early CP detection, availability and access to neuroimaging can be problematic. In the U.S., MRI at term age equivalent for neonatal intensive care unit (NICU) patients is still not standard practice at most institutions [65]. Even in cases of clinical concern, the need for MRI must be extensively justified when considering payor reimbursements to parents and, in lower level NICUs, may involve the approval of transfer costs [65]. Access to MRI can be equally challenging for children identified in the community at later ages, representing up to one half of all children who develop CP.

While all the previously described barriers stem directly from implementation of guidelines into practice, another type of concern is emerging due to the very manner in which guidelines are developed. A systematic review of the best research evidence is the most rigorous way to derive the basis for implementation initiatives. However, as has been previously demonstrated, research findings benefit from establishment of external validity [66] or generalizability,

for example through Plan-Do-Check Cycles or other forms of reporting on clinical practice results [67]. As for all tools or interventions, a distinction exists between efficacy (the ability of something to work under ideal circumstances) and their effectiveness (the ability of something to work in real-world conditions) [68]. In the case of early detection of CP, the predictive validity of assessments used in select research populations by highly trained researchers can be altered when used in heterogenous clinical settings by providers with varied backgrounds and levels of training. Recent examples include the use of GMA patterns, HINE cut-off scores and MRI findings (or lack thereof) in mixed clinical populations, performed by clinicians during regularly scheduled visits vs. researchers who may use combinations of laboratory-based and clinical visits in their published studies [43, 69–72]. The predictive accuracy, and therefore predictive validity, of the recommended assessments for CP in daily clinical settings may thus appear to be lower than in published studies, not diminishing the value of the assessments but rather adding a layer of complexity to diagnosis certainty and disclosure.

6. The why of early detection for CP: Early intervention

In balancing all the concerns and complexities involved in giving an early diagnosis of CP lies the necessity of referring infants for targeted, effective and safe interventions to change developmental trajectories during a period of optimal plasticity. Over the past twenty years, several systematic reviews in multiple domains of impairment associated with CP [73] beyond the motor component of activity limitations have been published. They range from daily living activities (feeding, sleeping) [74, 75] to the senses (hearing, vision) [76, 77] to child and family wellbeing and environment (pain, spasticity and tone management, orthotics, parent mental health and parenting) [78–80] and developmental functions (communication, cognition) [81].

A recent follow-up consensus article from the IMPACT group included many of these systematic reviews published prior to 2020 [82] to begin supporting providers for infants and toddlers with CP on best practices, with indicators of quality of the evidence behind recommendations. These were grouped into three themes: skills development, complication prevention and parent support. The only strong

recommendations in support of interventions were skills development to improve motor function and cognition. For CP, strong recommendations were stated against certain types of alternative practices for sleep, passive movement-based motor interventions and generic early developmental intervention, due to lack of efficacy or safety concerns. Most interventions had "conditional" recommendations for use, due to the quality of the evidence or the imprecision of extrapolation evidence from other populations (e.g., very preterm infants).

The consensus statement both helped promote interventions that work and underscored the gaps in knowledge in many domains for children under age two. This work was complemented by a set of systematic reviews published later that year, which engaged over 400 parents and patients with CP through a large qualitative survey to guide recommendations for sleep, pain and spasticity management in the under two with or at high-risk for CP [75, 78, 80]. The findings highlighted gaps between practice, evidence and parent preferences, prompting the editor to write a special commentary stating:

"Together these articles provide a sobering view of where we stand in treating young children with cerebral palsy. Much of what is now being done is difficult to support. . . . The notion that cerebral palsy cannot be effectively studied in infants is utter nonsense. These define a baseline state of affairs that is no longer acceptable. If we cringe at that baseline, we need to improve it" [83].

Beyond the need for more research in early interventions for CP, the certainty remains that early identification is critical to the development and research of new, improved interventions leveraging an optimal period of brain and body neuroplasticity to change outcomes into adulthood. While some have argued (prior to new evidence) that there is no point in early detection as no specific interventions exist beyond the general state early intervention services, this is a nihilistic and self-defeating prophecy: without early detection, there can be no development through research of more effective, safer and specific treatments for CP or CP spectrum disorders.

7. Parent perspectives on "High-Risk for CP" designation

The CPF, along with U.S. and Australian researchers, conducted a day-long parent focus group

amongst parents of children with CP with varied experiences in receiving the diagnosis. One of the topics discussed was how parents would perceive being told their child had a "High-Risk for CP" designation from a medical provider. Clearly explained were the uncertainty inherent to the term, the distinction between a designation and a diagnosis (one being descriptive terminology vs. the other corresponding to a diagnostic and billing code in the healthcare system). Thematic analyses were conducted, and these results were published in 2019 [84]. The perception of the designation was that it was an acceptable alternative, with the idea that the conversation surrounding the diagnosis would continue and might be revisited. Additional review of transcripts from the day revealed parent direct quotes such as:

From a parent who did not receive the "High-Risk" designation and had to wait several years before finding out what was happening with his child:

"So, that's why no-one could really even say anything to us until after two . . . But I felt like I was . . . I felt like he was cheated. Because I didn't have this opportunity with these tests, or even the thought thrown out to me that, "Hey, your son might have CP and we have this much of a percentage, this is what we can try to start doing for you now." I think that if I'd had that opportunity, my son would have so much more progression because he would have had those opportunities to be in there earlier."

From a parent, addressing the uncertainty inherent to the designation and the possibility that it might not be CP in the end:

"Allowing you to say it's okay to make mistakes, . . . is so important, and I think that's what the dialog needs to get to. We need to be able to have these conversations where people feel comfortable having someone else in the room, where people feel comfortable if somebody is crying to give them a moment to get through it, and then to come back in language that everybody understands."

And from another parent, on the same topic:

"Like she said earlier, it's okay to make mistakes. You're human."

8. Conclusion

The designation of "High-Risk for CP" adopted by more than 150 providers throughout North America and beyond, serves as a pragmatic compromise between the need to provide the best and earliest clinical care, at the same time as we strive to implement the highest levels of evidence acquired through carefully designed and protocolized research studies. As for all compromises, it results in an imperfect and less directive approach. However, medicine (outside of the surgical operating room) rarely occurs in carefully controlled circumstances. Most of the time, medical knowledge scaffolds decision-making and care with a cognitive framework to assist practitioners in managing the chaos of illness, interruptions and disruptions to health and development. Until more evidence emerges, classical research studies along with implementation science will help refine the usefulness of this "High-Risk for CP" designation. For now, the designation can be used to refer infants to the interventions they may benefit from, encourage parents towards the supports they need, and provide families with opportunities to participate in the research studies that will allow development of new and better interventions for CP.

Acknowledgments

The CNFUN Steering Committee has decided to endorse the consensus statement on High-risk for CP.

Supplementary material

The supplementary material is available in the electronic version of this article: <https://dx.doi.org/10.3233/PRM-220030>.

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