

Short Communication

Improving Care and Empowering Adults Living with SMA: A Call to Action in the New Treatment Era

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Abstract. While Spinal Muscular Atrophy (SMA) has historically been managed with supportive measures, the emergence of innovative medicines has given those living with SMA hope for improved quality of life and has revolutionized care. Despite these advances, the use of therapies and changes in disease management strategies have focused on pediatric populations, leaving adults living with SMA, and those transitioning into adulthood, relatively neglected. Through a multi-faceted approach that gathered unbiased perspectives from clinical experts, validated insights from individuals with lived experiences, and substantiated findings with evidence from the literature, we have exposed unmet needs that are hindering the field and, ultimately, impacting care and quality of life for adults living with SMA. Here, we set new aspirations and calls to action to inspire continued research in this field, stimulate dialogue across the SMA community and inform policies that deliver effective management and care throughout an adult's journey living with SMA.

Keywords: Adults living with SMA, Burden of Disease (BoD), health services, lived experience, Neuromuscular Disease (NMD), Quality of Life (QoL), Spinal Muscular Atrophy (SMA), transition

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INTRODUCTION

Supportive care is the cornerstone of clinical management in Spinal Muscular Atrophy (SMA). The emergence of disease-modifying medicines (e.g. nusinersen, onasemnogene abeparvovec-xioi, risdiplam) has delivered options that have improved survival rates for the most severe forms of the disease [1], offered hope for a longer and improved quality of life (QoL) and impacted care paradigms. The application of therapies, the transformation of disease management strategies and evolution of related policies have primarily focused on pediatric populations. While everyone should feel proud of these accomplishments, adults living with SMA and those transitioning into adulthood have been relatively neglected, despite emerging studies focused on this group [2–4] and some advances in the field (e.g. improved respiratory care [5], home adaptations [6], and devices that allow for greater independence, such as power wheelchairs and voice amplifiers [7]).

As more individuals transition into adulthood and an increasing number of adults—energized by the potential of newly available treatments—(re-)engage with health systems [8], there is an opportunity, indeed, an imperative, to do more for this underserved population. Our systems and support structures must further evolve if we are to maximize the value and benefit of medical advances and ensure that adults living with SMA have the highest level of care and support. Through this, we can not only relieve the burden of SMA on individuals and society (e.g. the economic impact [9]) but, importantly, also enhance individuals' quality of life, where even those with severe disease (e.g. non-ambulatory) can achieve a desired standard of living.

The aim of this publication is to set a bold ambition for the field by defining an aspirational state for the care, management and support of all adults living with SMA. We hope that by setting this vision, we can inspire future research that fills knowledge gaps, stimulates critical dialogue across the SMA community and drives concerted discussions on future policies that bring us closer to a common objective.

To do so in a meaningful way, we explored our personal viewpoints, building on years of experience working with those living with SMA, and validated findings with evidence from the literature and, importantly, with patients and patient advocates themselves (see Box 1 for details).

Based on this, we believe there is an opportunity to evolve our systems and support structures to

Box 1. Overview of our approach

For this commentary, we i) gathered unbiased perspectives from our group of clinical SMA leaders, ii) substantiated (or countered) our views with published evidence, and iii) validated our perspectives with patients and patient groups. First, we conducted a modified Delphi approach, holding one-on-one interviews with co-authors to gather perspectives on unmet needs, system gaps and socioeconomic impact of SMA. In parallel, a literature review was conducted to gather supporting (or countervailing) evidence, though data relevant to adults living with SMA are sparse, emphasizing the need for our commentary. All insights were then presented to the group to prioritize findings, which were then bucketed and extrapolated into three major aspirations.

We tested our findings with a group of ~30 stakeholders from Europe, Canada and the United States—including adults living with SMA, patient advocates and other clinicians. Through this roundtable discussion, we validated aspirations, rationale and calls to action, and received nuanced feedback from the voices of individuals with lived experiences, which we've reflected here.

be more *age-appropriate, comprehensive, integrated and robust* so that they can be more *meaningful, enabling and empowering* for adults living with SMA—and in many cases, adults more broadly living with neuromuscular disorders (NMDs). As such, we have defined three long-term aspirations aimed at enhancing systems and structures for adults living with SMA *in the treatment era*:

1. Provide *age-appropriate and comprehensive* care that delivers the most *meaningful* health outcomes and QoL for adults living with SMA.
2. Establish more *integrated* pathways that *enable* adults living with SMA to optimally manage their multifaceted healthcare needs.
3. *Strengthen* social and financial support systems that *empower* adults living with SMA and their caregivers to fulfill their personal goals.

Recognizing that these aspirations will take time, we acknowledge the health challenges resulting from COVID-19 as patients with chronic illnesses face delays in follow-up and public resources for healthcare potentially decline. However, it is our belief that we must act now, because in many ways, these

aspirations will endure and take on new meaning as our approach to SMA disease management evolves. Below, we detail each aspiration, describe needs that must be addressed and set calls to action that can bring us closer to our common vision.

ASPIRATION #1. PROVIDE AGE-APPROPRIATE AND COMPREHENSIVE CARE THAT DELIVERS THE MOST MEANINGFUL HEALTH OUTCOMES AND QOL FOR ADULTS LIVING WITH SMA

To date, our ability to provide age-appropriate, comprehensive care for adults living with SMA has been challenged by i) gaps in our understanding of the health challenges, limiting our ability to anticipate needs, ii) low level of appreciation for the most meaningful clinical and QoL outcomes, impacting how we assess and monitor progress, and iii) a lack of access to the right specialists and tools, hampering our ability to address all needs.

We need a deeper understanding of the health challenges faced by adults living with SMA

Adults living with SMA can face unique health challenges that require solutions pediatric approaches cannot necessarily address. Beyond core symptoms (e.g. respiratory, motor function), clinical issues that can be more prominent in adults include excessive fatigue [10], kidney stones, osteoporosis, acidosis [11], hypertension [12], weight management, sexual health and hormonal issues. Often, adults also receive inadequate reproductive health advice, for example, being told that having a child is not possible/too dangerous despite many adults having uneventful pregnancies [13]. Additionally, some clinical challenges experienced in childhood (e.g. scoliosis) may stabilize prior to transitioning into adulthood [14]. While standards of care (SOCs) for managing SMA have been developed [15, 16], they are primarily based on pediatric best practices, which may overlook considerations for adults. To tailor SOCs, we need to deepen our understanding of disease progression alongside the aging process. We call for more longitudinal studies in the treatment era that enable better prediction of the multifaceted challenges faced by adults and clinical/real-world studies that can evaluate benefits of supportive care (e.g. exercise, rehabilitation).

Given the heterogeneity of SMA in adult populations—which will become more heterogeneous as

more individuals transition into adulthood—age-appropriate and comprehensive care will only be possible with greater knowledge of the disease across the patient journey, differences among sub-populations and issues facing adults.

We need to understand the most meaningful clinical and QoL outcomes for adults living with SMA

Age-appropriate care will require a deeper appreciation for meaningful clinical outcomes for adults living with SMA—both physical and psychological—and their impact on QoL. Independence and autonomy are recognized as drivers of QoL, allowing adults living with SMA to participate in daily activities, engage in personal relationships, care for children and contribute to their desired degree at work, school or social life [17–19]. Stabilization of the disease, which has different meanings depending on severity (e.g. motor function in walkers, finger movements and preserved ventilation in severe forms), can often allow individuals to maintain that autonomy [10], yet it is not always recognized as a success marker. In addition to addressing physical function, we must also focus on the psychological difficulties (e.g. depression, anxiety) that impact QoL and patient engagement [20]. Indeed, adults diagnosed in adulthood may at times experience greater mental health challenges compared to those entering adulthood with the disease [21], and these challenges are particularly acute when all adults living with SMA experience a major change in disease progression (e.g. loss of motor function, respiratory machine dependence).

To measure progress against outcomes of interest to patients, and provide more age-appropriate care, we call for an evolution of more age-appropriate assessment frameworks that better reflect adult (and disease) circumstances. The customization should focus on disease severity versus more traditional classification of ‘SMA type’—given the range of phenotypes observed—, be more sensitive to clinical outcomes most meaningful to adults (e.g. mobility, pain, mental health) and better align with patient-reported quality of life outcomes (e.g. autonomy, wellbeing) [18, 22, 23].

We need to provide access to supportive care and innovative medicines

Given SMA’s multifaceted nature, adults require support from many professionals, including neu-

rologists, physiotherapists, nutritionists, respiratory therapists, speech therapists, gynecologists, urologists, psychotherapists, psychiatrists, occupational therapists, dentists and primary care providers (i.e. general practitioners, family doctors and nurse practitioners). However, specialists are often not available due to time or access limitations (e.g. payer reimbursement). Physical barriers can also impact access as many adults, especially those dependent on a wheelchair, are challenged to enter clinics or receive specialized investigations (e.g. imaging), notwithstanding some structural modifications to enhance access for those with NMDs (e.g. rehabilitation centres). Where adults can access specialists, there is often a lack of experience treating SMA. We call for capacity-building through education, training, and sharing of best practices and facility adaptation to ensure adults receive appropriate care.

Limited access extends to innovative medicines, notwithstanding recent evidence suggesting benefits in adults [24–26] and a desire for treatments [27]. While adults living with SMA are participating in trials, fundraising for research and advocating for access, most (81.3%) feel that a lack of access to medicines contributes to a low perceived value of care and reduced desire to engage in disease management [19]. As a result, we are likely underestimating disease prevalence and the need for services, further limiting the ability of adults to achieve what is most meaningful to them. In the future, clinical trials need to include adults living with SMA and representative subpopulations to generate further evidence demonstrating the benefit of treatments for *all* groups [28]. We call for more favorable policies and approaches that improve access to innovative medicines based on clinical evidence and the overall value of treatments for adults.

Overall, we believe with enhanced knowledge of SMA in adult populations, a deeper appreciation and integration of clinical and QoL outcomes, and greater access to supportive measures and innovative medicines, we can deliver age-appropriate and comprehensive advice and care that generates more meaningful outcomes for adults.

ASPIRATION #2. ESTABLISH MORE INTEGRATED CARE PATHWAYS THAT ENABLE ADULTS LIVING WITH SMA TO OPTIMALLY MANAGE THEIR MULTIFACETED HEALTHCARE NEEDS

Unlike pediatric environments, adults living with SMA face fragmented care pathways, which leads

to challenges in navigating systems. This is particularly problematic during the transition from pediatric to adult care. Moreover, while the lack of digital solutions is not specific to the experience of adults living with SMA, these tools can provide benefits by enabling consistent engagement in disease management.

We need to reduce barriers to navigating complex health systems

Leading health systems around the world have established multidisciplinary clinics to ensure access to coordinated treatment and care for adults living with SMA (and other NMDs). However, healthcare is often fragmented [2] and spread across different sites/hospitals, posing a challenge to those working full-time (given absence from their job) and those living in remote regions (given travel requirements) [29]. Systems are therefore placing the onus on adults living with SMA to navigate their needs, despite the fact that many are well-informed regarding their condition and patient advocates offer strong support. What often results is adults living with SMA engaging solely with their GP or a specialist that can address an immediate concern (e.g. neurologists for walkers, pulmonologists for sitters). We therefore call for policies that lead to more coordinated approaches to care (e.g. through single-site clinics, dedicated care managers as points of contact). By doing so, we can foster an individual's willingness to sustain engagement. We acknowledge that mechanisms to integrate pathways will differ by jurisdiction.

We need to optimize the transition from pediatric to adult care

The impact of fragmented care can be exacerbated for those transitioning from pediatric to adult care, due to the high level of coordinated support received in pediatric settings. It has been reported that those transitioning from pediatric to adult healthcare services experience difficulties in navigating a complex health system and engaging with new specialists, often describing the experience as “challenging and scary” [2]. Furthermore, adults living with SMA can also experience challenges during this transitional period, specifically when having to move away (e.g. for post-secondary education), which requires a patient to join a new care network. While not widespread across the SMA community, some jurisdictions have recognized this challenge

and have implemented specific practices to alleviate this impact (e.g. transitional clinics where both adult and pediatric clinicians attend appointments [30]). We call for greater adoption of best practices and dedicated processes (e.g. formal transitional care clinics, communication pathways between pediatric and adult specialists, national network of specialists) that facilitate the transition to adult care and knowledge transfer.

We need to incorporate technological advancements that facilitate (re-)integration of adults living with SMA into the health system

Modernizing health systems through the integration of digital tools can enable patient engagement and care delivery, a phenomenon that has been accelerated because of COVID-19. While we agree with other clinical experts that in-hospital treatments for SMA should not be considered elective [31], some functional assessments (e.g. symptom verification, diet assessment) [32] that are now occurring via telemedicine may be sustainable approaches to decrease disruption for adults living with SMA (also applicable to children with SMA and their caregivers). Moreover, the use of advanced technologies (e.g. apps, wearables) to collect data are slowly being adopted [33, 34]. COVID-19 will likely accelerate their use, which may expose opportunities to optimize care (e.g. providing at-home exercise routines, conducting remote check-ups), enhance research efforts, and ultimately enable adults living with SMA to optimize their disease management approach in ways that better meet their needs and those of their caregivers. We therefore call for integration of value-adding digital tools that allow patients to (re-)engage and/or (re-)integrate into the health system.

Overall, we believe that with the development of more integrated pathways, particularly at the point of transition, and the incorporation of digital tools, we can better enable adults living with SMA to optimally manage their multifaceted needs.

ASPIRATION #3. STRENGTHEN SOCIAL AND FINANCIAL SUPPORT SYSTEMS THAT EMPOWER ADULTS LIVING WITH SMA AND THEIR CAREGIVERS TO FULFILL THEIR PERSONAL GOALS

As treatment and care paradigms evolve, we cannot forget the criticality of social and financial support systems in empowering adults living

with SMA to fulfill personal goals. Our ability to strengthen these systems is confronted by societal barriers placed on adults living with SMA—be it social stigmas/stereotypes, daily physical challenges or financial burdens. We must acknowledge that these physical, psychological and financial challenges also impact caregivers, who can often be family members (e.g. a spouse, child, sibling or parent) managing stresses of their own unrelated to care of their loved ones living with SMA.

We need to tackle the societal barriers that impede adults living with SMA

Many adults living with SMA have a positive outlook on life and overcome the challenges associated with their disease, including participating in social activities [35, 36], gaining employment [35, 37] and pursuing post-secondary education. Yet, despite many adults living with SMA having a high degree of intellectual and emotional resilience [2, 38], they often experience societal barriers—be it social stigma (e.g. around physical/intellectual capacities [2]) or daily physical challenges—that can impact morale and influence decisions [36]. Furthermore, physical obstructions (e.g. accessibility into buildings, public restrooms) complicate daily tasks and significantly impact an individual's psychosocial wellbeing and willingness to participate. While existing initiatives have helped adults prosper (e.g. YouTube channels for tips, tools to improve psychological health like mindfulness exercises), accessibility continues to be a critical challenge. We call on policymakers to enhance social services that are easily navigated and accessed by adults and accessibility policies that can impact the lives of those with SMA (and others with disabilities). We also call for greater promotion of patient-driven community networks to share knowledge and best practices, discuss experiences, empower the patient and caregiver voice, and provide support for adults living with SMA via online portals and books/pamphlets on pressing topics (e.g. raising children, sexual health).

We need to address the physical, psychological and social impact of SMA on caregivers

The physical, psychological and social impact of SMA often extends to primary caregivers of adults living with SMA. This impact can be high, long-lasting and progressively worsens with age, due in part to the physically demanding nature of the care [39]. Beyond the physical demands of caring for an

adult living with SMA, caregivers can also experience an impact of the disease on their own psychological (e.g. emotional wellbeing, sleep disturbances), social (e.g. ability to perform daily activities, such as chores or seeing friends, interacting with family members) and financial wellbeing [39]. We need to deepen our understanding of the implications of this dedication as well as the opportunity costs to society in order to truly appreciate the broader implications and impact of SMA. We call for specific assessments of the socioeconomic implications of SMA on caregivers to provide an evidence-informed proposal for decision-makers around funding and support.

We need to relieve the financial impact of SMA on adults and caregivers

The financial impact of SMA is high and increases with disease severity, with a significant portion of this impact due to indirect costs (e.g. informal care costs, productivity loss) [9, 40]. In private systems, medical decisions are impacted by financial considerations; for example, research has shown that up to 33% of adults living with SMA experienced delayed medical care due to high costs [41]. Further, unlocking (often insufficient) support that is available (e.g. for wheelchairs, car adaptations, home modifications) is tied to income thresholds that impact the decisions made by adults living with SMA and their caregivers regarding care and support, daily living and professional pursuits. When considering the unique needs of the adult population (e.g. education, employment, childcare support), our understanding of SMA's financial impact and the effectiveness of existing financial tools remains low, limiting our ability to advocate for those that deliver benefit. We call for assessments of financial support structures that account for the patient, caregiver and community voice and identify evidence-based options that are positioned to empower adults living with SMA and their caregivers to accomplish their personal goals.

Overall, we believe there is an opportunity to empower adults living with SMA and their caregivers by tackling societal barriers, addressing the impact on caregivers and accounting for the contribution those with SMA have on intellectual and economic growth with proper financial support.

CONCLUSION AND FUTURE PERSPECTIVES

Our aspirational statements will take time, yet we cannot afford to sit idle as we progress into the

treatment era. While our calls are high-level, they are intended to stimulate discussion, move us closer to our long-term aspirations and, most importantly, ensure adults living with SMA and their caregivers can achieve what is most meaningful to them (Table 1). By setting the stage for action and working with advocacy partners, stepwise, near-term progress can be made towards these aspirations. Over the long-term, we can realize a more meaningful, enabling and empowering world for adults living with SMA. We look forward to engaging with the community and policymakers to help make this vision a reality.

CONFLICT OF INTEREST

MCW has served on advisory boards/given consultancy for and received travel or speaker honoraria from Ask Bio, Avexis, Biogen, Fulcrum, Novartis, Pharnext, PTC, Roche, Santhera, Sarepta and Wave Live Sciences. **CAC** has received grant support from Avexys, Biogen, Roche, and NIH, served on advisory boards for Avexys, Biogen, Roche, Genentec, Cytokinetics, and PTC, and received speaker honoraria from Biogen; **TD** has served on advisory boards, speaker honoraria or consulted with Roche, Biogen, Scholar Rock, Novartis, Avexis, Sarepta; **NG** has served on advisory board for Biogen, Roche and Avexis, received speaker honoraria from Biogen and Roche; **AM** has served on advisory boards for Regenxbio, Sarepta, Biogen and Roche and have been in the past for Summit and PTC and is a consultant trainer for outcome measures for Avexis, Roche and Biogen; **MO** has received institutional research support from Biogen and Roche; **RQ** has served on advisory boards, data monitoring committees and received honoraria from: TRINDS, PTC therapeutics, Sanofi- Genzyme, Sarepta, Santhera and Roche; **JV** has served on advisory boards or consulted otherwise for Biogen and Roche; **JFVC** has served on advisory boards for Biogen and Roche, received travel or speaker honoraria from Biogen and Roche; **LS** has served on advisory board/given consultancy for Biogen, Roche and Avexis.

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Table 1
Long-term aspirations and calls to action

Aspiration	Recap of calls to action
Provide age-appropriate and comprehensive care that delivers the most meaningful health outcomes and QoL for adults living with SMA.	<ul style="list-style-type: none"> • Conducting more longitudinal studies in the treatment era that enable better prediction of the multifaceted challenges faced by adults and clinical/real-world studies that can evaluate benefits of supportive care (e.g. exercise, rehabilitation). • Evolving assessment frameworks to better reflect adult (and disease) circumstances (e.g. age-appropriate tests according to disease severity), to be more sensitive to clinical outcomes most meaningful to adults (e.g. mobility, pain, mental health) and to align with patient-reported quality of life outcomes (e.g. autonomy, wellbeing). • Capacity-building through education, training, and sharing of best practices and facility adaptation to ensure adults receive appropriate care. • Establishing more favorable policies that improve access to innovative medicines that are based on this evidence and the value for adults.
Establish more integrated pathways that enable adults living with SMA to optimally manage their multifaceted healthcare needs.	<ul style="list-style-type: none"> • Advocating for policies that lead to more coordinated approaches to care (e.g. through single-site clinics, dedicated care managers as points of contact). • Integrating best practices and dedicated processes (e.g. formal transitional care clinics, communication pathways between pediatric and adult specialists, national network of specialists) that facilitate the transition to adult care and knowledge transfer. • Integrating value-adding digital tools that allow patients to (re-)engage and/or (re-)integrate into the health system.
Strengthen social and financial support systems that empower adults living with SMA and their caregivers to fulfill their personal goals.	<ul style="list-style-type: none"> • Enhancing social services that are easily navigated and accessed by adults and accessibility policies that can impact the lives of those with SMA (and others with disabilities). • Promoting patient-driven community networks to share knowledge and best practices, discuss experiences, empower the patient and caregiver voice and provide support for adults living with SMA via online portals and books/pamphlets on pressing topics (e.g. raising children, sexual health). • Assessing the socioeconomic implications of SMA on caregivers to provide an evidence-informed proposal for decision-makers around funding and support. • Evaluating financial support structures that account for the patient and community voice and identify evidence-based options that are positioned to empower adults living with SMA and their caregivers to accomplish their personal goals.

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ROLE OF FUNDER/SPONSOR

Beyond sponsoring Shift Health to manage a study focused on adults living with SMA, the concepts, scope and details were not defined in any way a priori by F. Hoffmann-La Roche Ltd and are solely the viewpoints of the co-authors. In order to protect and maintain this study's independence and credibility, F. Hoffmann-La Roche Ltd was completely hands-off in this effort and did not engage with co-authors on this matter over the course of data collection and manuscript development. Finally, F. Hoffmann-La Roche Ltd was not privy to the direction of, or content in, the manuscript until it was published.

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