



Introducing the WHO ICOPE approach into HIV care: A perspective on healthy ageing in people living with HIV

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ABSTRACT

Background: The ageing of people living with HIV (PWH) presents unique clinical and public health challenges that are not fully addressed by current care models.

Objective: This Perspective paper aims to explore the feasibility and added value of introducing the World Health Organization (WHO) Integrated Care for Older People (ICOPE) framework and guidelines into HIV care models, using the lens of intrinsic capacity (IC) and functional ability to reframe how age-related conditions are managed. In particular, we discuss how HIV services can adopt intrinsic capacity (IC) assessments and function-centered care as a scalable strategy to promote healthy ageing.

Methods: This is a narrative and conceptual Perspective based on literature review, expert consultation, and clinical case examples, including the Modena HIV Metabolic Clinic and experiences from resource-limited settings.

Results: The ICOPE approach offers a feasible, person-centred framework for identifying and managing early declines of IC across six domains. ICOPE facilitates timely interventions at the primary health care level. HIV care services and systems, already oriented towards longitudinal and multidisciplinary management, are uniquely positioned to pioneer ICOPE implementation.

Conclusion: HIV medicine may serve as a model for expanding the integration of the ICOPE approach across chronic diseases, especially in low-resource settings where primary care structures must address age-related vulnerability. Adopting ICOPE can promote healthy ageing in PWH and beyond.

1. Background

1.1. Section highlights and objective

This is a Perspective paper aiming to explore the feasibility and added value of introducing the World Health Organization (WHO) Integrated Care for Older People (ICOPE) framework and guidelines into HIV care models. While HIV medicine has already demonstrated innovation in managing chronic conditions and addressing age-related challenges, it has yet to fully adopt the ICOPE model. ICOPE is a broader, community based model aiming to optimize functional ability by addressing residual physical and mental capacities. Given the growing burden of multimorbidity, frailty, and psychosocial vulnerability among older people with HIV (PWH), this paper argues that HIV care offers a promising entry point for the integration of the ICOPE

approach. In particular, we discuss how HIV services—supported by well-developed infrastructures and a history of community-based interventions—can adopt intrinsic capacity (IC) assessments and function-centered care as a scalable strategy to promote healthy ageing [1,2].

1.2. Rethinking ageing: from frailty to functional ability

Ageing is a continuous, non-linear biological process shaped by life-long interactions of genetic, behavioural, and environmental factors [3]. At a biological level, these cumulative influences drive molecular and cellular changes such as mitochondrial dysfunction, genomic instability and chronic low-grade inflammation that progressively erode functional reserves. At a clinical level, it involves a progressive physical and cognitive decline, leading to increased vulnerability to stressors and

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disease [4]. It should be noted that ageing is not synonymous with disease or disability.

In the context of PWH, conventional indicators of ageing, such as chronological age or the presence of age-related non-communicable diseases, may be inadequate. Comorbidities alone do not capture the full complexity of ageing [5]. Frailty, a multidimensional syndrome reflecting reduced resilience to stressors and impaired homeostasis, is a more accurate and comprehensive measure [6]. It encompasses physical, psychological, and social domains, and better predicts adverse outcomes such as hospitalization, disability, and mortality. Therefore, in recent decades, ageing has been more commonly characterized by frailty than by the mere presence of chronic diseases. Frailty in PWH is a highly prevalent and clinically significant condition that appears earlier in life compared to the general population [7,8]. It reflects the accelerated biological ageing that characterizes HIV infection, even in individuals on long-term antiretroviral therapy with virological suppression [9]. The mechanisms underlying frailty in PWH are multifactorial, including chronic immune activation, mitochondrial dysfunction, and persistent systemic inflammation [10].

Frailty has long served as a useful concept to characterize vulnerability and physiological decline in ageing populations, including PWH [11,12]. However, the WHO has called for a shift from deficit-based models, such as frailty, toward a more empowering and actionable framework of healthy ageing centered on IC [13]. This shift is not only semantic, but also reflects a reorientation of health systems from reacting to deterioration towards a proactive promotion of resilience, autonomy, and function.

Healthy ageing, as defined by WHO, is “the process of developing and maintaining the functional ability that enables well-being in older age” [14]. This formulation is based on the interaction between IC and the environment that supports an individual in doing what they value. Unlike frailty, which tends to label decline and dependence, IC emphasizes strengths and residual capacities. It provides a universal language for monitoring health trajectories, setting goals, and identifying actionable areas for intervention [13,15].

1.3. Why ageing is different in people living with HIV

Ageing in PWH is a biologically, clinically, and psychosocially distinct phenomenon. At the biological level, HIV infection, even when controlled with ART, leads to chronic immune activation, inflammation, and cellular senescence [16]. These mechanisms contribute to accelerated ageing processes, increasing the risk of age-related diseases such as cardiovascular disease, osteoporosis, neurocognitive impairment, and cancers at a younger age than in HIV-negative individuals [17,18].

At the clinical level, PWH experience a higher burden of comorbidities and geriatric syndromes such as frailty, sarcopenia, and polypharmacy [10]. The management of these conditions is complicated by potential drug-drug interactions and the lack of HIV-specific guidelines for older adults [10,19]. Furthermore, early exposure to older-generation ART has left some long-term survivors with irreversible toxicities [20].

At the psychosocial level, ageing with HIV is often accompanied by elevated rates of depression, anxiety, and social isolation [21,22]. PWH are more likely to live alone, have reduced family support, and experience compounded stigma related to both HIV and ageing [21]. Socio-economic disadvantages and life-long exposure to discrimination exacerbate these challenges.

The cumulative burden of adverse social determinants of health also contributes to a heightened risk of future cognitive decline and dementia [23]. Thus, ageing in PWH is not simply a matter of chronology, but the result of a complex interplay of biological damage, clinical complexity, and social adversity. Responding effectively requires a multidimensional, person-centred approach to care [5,24].

Older PWH face a distinct set of challenges that extend beyond medical complexity. One key issue is the limited availability of informal

caregiving networks. Many PWH, particularly gay men, may not have children or family members who can offer support in later life. This lack of familial caregiving structures increases their reliance on formal health and social services [25,26].

Compounding this is the pervasive experience of loneliness. Social isolation among older PWH is often driven by a combination of HIV-related stigma, ageism, and the loss of peers. Loneliness has been shown to correlate with worse mental and physical health outcomes, including depression, cognitive impairment, and reduced adherence to care [22,24]. Qualitative studies underscore that feelings of invisibility and exclusion from both the HIV community and the broader ageing population are common [27].

These realities highlight the urgent need for community-based interventions, age-inclusive HIV care models, and policies that recognize the intersectional vulnerabilities of this population. A holistic approach must include psychosocial support, mental health services, and structural changes to ensure older PWH can age with dignity, connection, and care [28].

This Perspective paper aims to explore the feasibility and added value of introducing the World Health Organization (WHO) Integrated Care for Older People (ICOPE) framework and guidelines into HIV care models, using the lens of IC and functional ability to reframe how age-related conditions are managed. In particular, we discuss how HIV services can adopt intrinsic capacity (IC) assessments and function-centered care as a scalable strategy to promote healthy ageing.

This is a narrative and conceptual Perspective based on literature review, expert consultation, and clinical case examples, including the Modena HIV Metabolic Clinic and experiences from resource-limited settings.

The Possible Role of Intrinsic Capacity in Contemporary HIV Care

Section highlights: In people living with HIV, functional ability is shaped by a combined impact of biological vulnerability and socio-environmental disadvantage, making intrinsic capacity assessment essential for personalized, proactive, and holistic care.

In the context of HIV care, this approach is particularly relevant. PWH often exhibit early and accelerated loss of IC due to comorbidities, inflammation, polypharmacy, and syndromes like sarcopenia. Yet biological ageing alone does not explain the functional vulnerability of older PWH. What widens the gap between IC and actual functional ability is the interaction with a disadvantaged environment [29].

PWH face specific environmental barriers—including adverse social determinants of health (e.g., poverty, housing instability, limited access to geriatric-sensitive services), persistent HIV-related stigma, and ageism. These intersecting forms of discrimination not only reduce opportunities for social participation and access to care, but also impact self-perception and health-seeking behavior. Stigma may lead to internalized shame and isolation, while ageism contributes to invisibility and neglect within both HIV and broader ageing communities [24].

Thus, the functional ability of older PWH is shaped by a “double burden”: biological vulnerability compounded by socio-structural exclusion. Assessing IC in this context enables earlier identification of decline, proactive rehabilitation, and the tailoring of care plans that integrate social and environmental supports.

At the clinical level, IC assessment provides a platform for personalized and anticipatory care strategies that preserve autonomy and quality of life [30]. At the public health level, it supports population segmentation, service design, and evaluation of long-term care models. Incorporating IC into HIV care pathways redefines success—not merely in terms of viral suppression, but in supporting older PWH to live meaningful, connected, and functional lives.

1.4. Pioneering innovations: HIV as a driver of reorientation of care

Section highlight: HIV care remains primarily focused on viral suppression, while integrated, function- and person-centered approaches are needed to address the broader needs of older PWH.

HIV medicine is one of the few clinical fields where the concept of frailty was introduced early, reflecting the unique ageing patterns observed in PWH [31]. This recognition helped lay the groundwork for what has been called the birth of "geriatric HIV medicine"—a term formalized in the seminal article *Geriatric HIV Medicine is Born* [31]. Despite this milestone, the discipline remains in its infancy. Most clinical pathways still prioritize viral suppression and comorbidity management, without adequately addressing geriatric syndromes, functional decline, or the psychosocial needs of older PWH.

Among the innovative experiences addressing this gap is the GEPPCO cohort, a prospective, multicenter study in Italy that brings together infectious disease specialists and geriatricians to jointly evaluate the health of older PWH [32]. The GEPPCO study investigates not only the specific challenges of ART in ageing populations but also the prevalence and impact of geriatric syndromes [33]. These include polypharmacy, drug-drug interactions, and tolerance profiles that are particularly enhanced in old age [34].

This integrated model represents a shift from disease-centered care to function- and person-centered care. It underscores that ageing with HIV extends beyond virologic control and addresses broader domains such as the preservation of independence, quality of life, and social engagement. However, such models remain uncommon and substantial efforts are still required to integrate them into routine practice. Building formal collaborations between HIV clinicians and multidisciplinary teams, promoting shared training, and embedding basic principles of geriatric medicine into HIV guidelines are essential next steps to advance this field from concept to care standard.

1.5. Translating guidelines into practice: the EACS experience

Section highlight: EACS guidelines address ageing in PWH, but limited training, resources, and multidisciplinary support slow their implementation in clinical practice.

The European AIDS Clinical Society (EACS) was among the first to introduce a dedicated section on the management of older PWH, marking a critical step forward in acknowledging and addressing ageing-related vulnerability. Recent updates in the guidelines further strengthened this commitment [35].

The formal inclusion of frailty assessment was first introduced in version 10.0 of the guidelines in 2019, using both the frailty phenotype and the frailty index as key tools. More recently, version 12 added a structured screening approach to frailty, with the aim of improving the early detection and management of age-related vulnerabilities of older PWH [35].

These guidelines emphasize that frailty should be used to trigger a comprehensive geriatric assessment (CGA), incorporating polypharmacy review, deprescribing, and identification of potentially inappropriate prescriptions. Tools like the STOPP/START criteria and the Beers' List are recommended to optimize pharmacological care in this population [36].

Despite these advances, implementation remains limited. Data from high-income countries suggest that only a minority of HIV centers routinely screen for frailty [37]. Despite the availability of simpler screening tools, such as walking speed or the Short Physical Performance Battery (SPPB), their uptake in clinical practice has remained limited. Additionally, a large cohort study showed that even when frailty screening is recommended for those over 50, age-based approaches alone miss a substantial proportion of frail individuals [38].

The major impediment is not merely technical but cultural. Many infectious disease physicians are not trained in geriatric principles and feel unprepared to perform CGAs. Furthermore, most HIV clinics lack established care models that include geriatric consultation or a true multidisciplinary team capable of evaluating and coordinating the broad range of social, cognitive, psychological, and physical needs of older PWH.

This gap is increasingly concerning as the HIV population ages.

Without adequate training and systemic integration of geriatric care principles, the vision of healthy ageing for PWH will remain out of reach. Addressing this will require both structural innovation and cultural transformation within HIV care delivery systems.

1.6. The ICOPE approach: A framework for person-centred HIV care

The WHO Integrated Care for Older People (ICOPE) approach offers a person-centred, community-oriented framework to manage age-related declines in IC. It is designed to promote healthy ageing by focusing on maintaining functional ability rather than solely managing diseases. ICOPE shifts clinical attention toward a set of core domains—mobility, cognition, psychological well-being, vitality/nutrition, vision, and hearing—that together comprise IC and whose impairments singularly represent risk conditions for care dependency [1,2,39].

In primary care, the ICOPE care pathway is structured around a sequential steps process: first, a basic screening of the six IC domains is conducted by non-specialist health workers or primary care professionals. Then, individuals with positive screening are referred for an in-depth assessment and development of a personalized care plan. This allows early detection of decline, planning of personalized interventions, and consistent implementation of the care strategies with monitoring and follow-up indications [1,39].

Assessing IC domains in older people can be considered analogous to checking vital signs in an emergency room: they serve as indicators of an individual's overall functional reserve and health status. Early changes in IC can foreshadow serious outcomes, and monitoring them regularly enables timely, often simple interventions that can preserve autonomy.

Adopting the ICOPE model within HIV care holds particular promise. Older PWH often have multidimensional needs that extend beyond virological control, including neglected but relevant aspects like hearing loss, vision impairment, and social disconnection. These domains are not only clinically relevant but also highly modifiable through low-cost interventions.

Unlike traditional frailty tools that may lack clear care pathways, ICOPE promotes a structured yet flexible approach that facilitates multidisciplinary response. It avoids rigid cut-offs, allowing for tailored assessments and interventions depending on context. Importantly, it also helps prevent the unintended use of frailty as a criterion for care limitation, a risk highlighted during the COVID-19 pandemic [40].

This model is not meant to replace frailty screening but to complement or precede it, especially in resource-limited or non-specialist settings where geriatric expertise may not be available. Integrating IC into HIV practice enables a continuum of integrated care and aligns with WHO guidance to promote healthy ageing.

Ultimately, ICOPE supports the concept that healthy ageing is not only a desirable aspiration but a fundamental goal of HIV care. It resonates with the UNAIDS "fourth 90 %" target: that 90 % of PWH should have an optimal quality of life with preserved function, autonomy, and well-being throughout the life course [41].

Implementing ICOPE in HIV Services: From Screening to System Integration

Section highlight: ICOPE offers a person-centred framework in HIV care, focusing on early detection of decline of functional ability, and tailored interventions to promote healthy ageing.

The second edition of the WHO ICOPE guidelines outlines a basic, scalable model of assessment that can be implemented at the primary care level [42]. This simplified evaluation strategy includes key domains of IC, making it well-suited for integration into HIV services.

A key strength of the ICOPE approach lies in its flexibility and capacity to be adapted across diverse healthcare systems. Whether primary care is delivered by general practitioners or by infectious disease specialists or by nurses in low middle income countries, the basic ICOPE assessment can be effectively integrated. Given that its structure has already been described, here we emphasize its clinical utility: once functional declines are identified through the basic assessment, the

approach provides a clear pathway for deeper evaluation and the implementation of targeted, individualized care plans.

Moreover, the HIV field offers a unique advantage: the presence of well-established, community-based networks. These networks comprise peer support workers, advocacy groups, and HIV-focused NGOs and can play a key role in the ICOPE referral system. By leveraging these community structures, it becomes possible to ensure follow-up, monitor functional trajectories, and co-create support plans that reflect the lived experiences of older PWH.

The real challenge is to move beyond siloed medical care and embed ICOPE as a shared platform across disciplines, including geriatrics, primary care, rehabilitation, mental health, and community services. In doing so, we can operationalize a person-centered model that is both feasible and impactful for older PWH.

A recent cross-sectional study conducted in South-Eastern Asia included 200 PWH aged 35 years and above attending outpatient care at the university clinic in Malaysia, alongside 101 community controls between 2021 and 2023. The WHO IC framework was adapted to assess functional domains. While overall IC scores were not significantly different between PWH and controls, PWH showed significantly lower cognitive function. Lower IC scores were independently associated with frailty, instrumental activities of daily living (IADL) deficits and elevated IL-6, with IC showing strong predictive accuracy for frailty in both initial Malaysian cohort and in an independent cohort of 275 PWH from Hong Kong. These findings support IC as a valuable tool to monitor overall vulnerability and aging trajectory in PWH [43].

Linking Assessment to Action: Operationalizing Interventions

Section highlight: Assessing intrinsic capacity enables timely, personalized, and scalable interventions that maintain or restore function, supporting independence and quality of life in older PWH.

The value of assessing IC lies in its ability to guide timely and personalized interventions to maintain or recover functional ability. IC domains are highly interconnected and improvements in one domain often generate cascading benefits across others. For instance, treating hearing loss can reduce cognitive load and improve social engagement, while enhanced nutrition may bolster vitality, mood, and mobility.

One of the main advantages of starting from IC rather than frailty is its operational simplicity. IC-based interventions can be delivered by a wide range of providers, including community workers and primary care physicians, without requiring a full multidisciplinary team and/or specialist competencies in geriatric medicine. Community-level actions include:

- Promoting self-care and self-management
- Using community-based services (e.g., social prescribing) for non-clinical support
- Addressing advanced illness and palliative care needs with dignity
- Delivering social care and home adaptations
- Supporting caregivers with respite, training, and emotional resources

Primary care physicians (including ID specialists in some settings) can:

- Define care goals based on the older person's values and preferences
- Find support in the management of chronic diseases, geriatric syndromes, and cardiovascular risks
- Conduct medication reviews for safety and adherence
- Offer multicomponent interventions (nutrition, exercise, social support)
- Provide vaccinations and routine preventive care

Supplementary Table 1 shows a framework of interventions based on impairments in specific IC domains or on frailty status.

Frailty-based models typically rely on a formal CGA, which requires a specific geriatric expertise. In many HIV centers, geriatricians are

absent and multidisciplinary teams may be rare or not adequately prepared. IC offers a scalable and inclusive model that supports action even in resource-constrained environments.

This proactive, capacity-oriented approach transforms HIV care into a platform for functional longevity. It supports a clinical culture where sustaining independence and quality of life is embedded as a standard goal for all ageing individuals with HIV.

1.7. Case study: the Modena HIV Metabolic Clinic

Section highlight: The Modena HIV Metabolic Clinic demonstrates how intrinsic capacity assessments, personalized care plans, and patient-engaged monitoring can operationalize person-centered HIV care for older PWH.

The Modena HIV Metabolic Clinic (MHMC) provides a concrete example of how IC can be integrated into HIV care. Older PWH attending the clinic undergo a two-level assessment strategy. Initial assessment identifies potential declines in IC domains, followed by a more in-depth geriatric evaluation when deficits are detected. This evaluation includes assessment of cognition (e.g., MoCA), mobility (e.g., SPPB), nutritional status (e.g., MNA), and mental health (e.g., CES-D and anxiety questionnaires). Supplementary Table 2 shows how IC is assessed with basic and in depth assessment.

A distinguishing feature of this approach is the generation of personalized radar graphs for each patient, which visually map the status of the six IC domains. These graphs are shared directly with patients and caregivers to enhance understanding, foster engagement, and track health trajectories over time. This visual communication supports shared decision-making and personalizes the conversation around priorities and actions. Supplementary figure 1 shows a clinical example of radar graphs from multidimensional evaluations of a patient with HIV.

The results of IC and clinical evaluation are also combined with patient-reported outcomes (PROs), such as measures of health-related quality of life (HRQoL), depression, loneliness, and psychological resilience. These tools provide a more complete view of the patient's lived experience and inform a truly person-centred care plan. In clinical practice, IC is used as a set of foundational "vital signs" from which clinical discussions begin. The IC profile serves as a launching point to explore targeted areas for intervention including physical, psychological, or social domains, by integrating objective assessment with patient-reported needs.

Together, these figures offer a visually intuitive profile of patient functioning. The figures are shared directly with patients to engage them in understanding and managing their own health.

The care plan developed at MHMC is dynamic and co-designed with the patient. Interventions are routinely reviewed and adapted over time to support autonomy and preserve function. This cyclical model of reassessment and refinement enables tailored strategies that respond to evolving clinical and personal priorities.

The MHMC experience demonstrates that ICOPE-guided care is feasible within a specialized HIV setting and adaptable to a multidisciplinary infrastructure. This model could be replicated in other

The ICOPE approach represents a global framework proposed by the WHO. However, adaptations to local contexts are essential to facilitate its implementation, enhance acceptability, and ensure long-term sustainability. The Modena experience illustrates how a similar strategy could be applied in other settings and countries with appropriate adaptations of assessment tools and care pathways with the aim of improving care to older PWH.

1.8. Reframing expectations: healthy living is possible in HIV

Increasing evidence shows that healthy ageing is possible in PWH, even with advanced age [41]. Some individuals with HIV have reached exceptional longevity (up to 100 years) while maintaining meaningful levels of autonomy and quality of life [44]. These cases demonstrate that

long life with HIV is not only achievable but can also be accompanied by preserved well-being [44,45].

The WHO ICOPE approach plays a critical role in supporting this goal. Its emphasis on person-centred care fosters active engagement from older individuals, helping them articulate their priorities and align care plans accordingly. Furthermore, ICOPE encourages the involvement of caregivers in both assessment and intervention, recognizing their importance in supporting adherence, safety, and emotional well-being [42].

Healthy ageing, as promoted through the integration of care for older people, thus becomes both a clinical target and a human right. It reinforces that HIV care should extend beyond viral suppression to the broader goals of autonomy, connection, and purpose throughout the life course. This aligns with the UNAIDS “fourth 90” objective: that 90 % of PWH experience a good quality of life [46].

1.9. Global lessons: applying ICOPE in resource-limited settings

In low- and middle-income countries, the rapid demographic transition and success of HIV treatment programs have created an urgent need to integrate ageing and chronic disease care [47]. Although access to geriatric expertise is often limited, the HIV infrastructure offers a valuable platform to expand services.

Pilot studies in countries such as Kenya, Uganda, and South Africa show that the ICOPE approach linked to community-based interventions is feasible when delivered even by trained lay health workers, eventually supported by digital tools. These efforts demonstrate that IC assessment can be incorporated into primary care through effective task-shifting.

HIV clinics already provide long-term care for chronic conditions like diabetes and hypertension, with systems in place for monitoring, referrals, and patient tracking. These existing capacities align with ICOPE’s design and make HIV clinics suitable for integrated geriatric care.

In the future, these platforms could also serve broader populations beyond PWH, offering a foundation to deliver ICOPE more widely. Their community engagement and multidisciplinary orientation position them ideally to pilot person-centred ageing care in primary care settings.

This model addresses the increasing convergence of HIV, ageing, and non-communicable diseases. Unlike most HIV-NCD integration efforts, which focus on single disease pairings, ICOPE provides a framework for broader functional assessments across multiple domains. By shifting from disease-specific management to function-oriented care, HIV services in LMICs can evolve into scalable entry points for healthy ageing—offering continuity, accessibility, and value across populations.

Some limitations of this Perspective paper must be acknowledged. This Perspective is based on a narrative rather than systematic review, and therefore may not capture the full scope of the literature. Evidence on the integration of ICOPE into HIV care remains limited and often context-specific, and most examples discussed derive from specialized settings without prospective data to identify and confirm clinical outcomes or generalizability across diverse healthcare systems.

2. Conclusion

Healthy ageing is not only a theoretical construct but an achievable outcome at both individual and population levels, particularly when care delivery is aligned with evolving needs of older PWH [46]. By shifting the paradigm from disease management to intrinsic capacity promotion, and from chronological age to functional ability, health systems can enable older PWH to live longer, healthier, and more fulfilling lives.

The ICOPE approach provides a practical and scalable framework to guide this transition.^{1,2} HIV medicine, given its longstanding experience in managing complex, multi-dimensional health issues and leveraging strong community-based infrastructures, may serve as a frontrunner in operationalizing ICOPE principles.

This approach is particularly relevant in resource-limited settings, where the HIV care infrastructure may represent the most viable structure to implement primary-care-oriented ageing models. In these contexts, ICOPE can help meet the growing need for integrated, person-centred care across the life course and across chronic conditions. HIV, once defined by stigma and crisis, may thus lead the way toward global models of healthy ageing for vulnerable populations.

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CRedit authorship contribution statement

Giovanni Guaraldi: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Jovana Milic:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Conceptualization. **Licia Gozzi:** Methodology, Investigation. **Severino Ambrosio:** Investigation. **Elisabetta Delmonte:** Investigation. **Irene Avanzini:** Investigation. **Barbara Castelnovo:** Writing – review & editing, Supervision. **Cristina Mussini:** Writing – review & editing, Supervision, Resources, Methodology.

Declaration of competing interest

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Supplementary materials

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