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Ageing with HIV: Clinical and Organisational Challenges of Care

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Abstract

Combination antiretroviral therapy (ART) has transformed human immunodeficiency virus (HIV) infection from a fatal disease into a manageable chronic condition; consequently, the population of people living with HIV (PLWH) is ageing rapidly. In many high-income settings more than half of PLWH are now aged 50 years or older. To characterise the clinical and organisational challenges that arise when HIV infection and biological ageing intersect, and to summarise the emerging models of integrated HIV-geriatric care intended to address them. A narrative review of English-language literature indexed in PubMed/MEDLINE was conducted, complemented by the current guidelines of the European AIDS Clinical Society (EACS) and the World Health Organization (WHO). Search terms combined the concepts of HIV, ageing,

multimorbidity, frailty, polypharmacy, neurocognitive disorders, cardiovascular disease and models of care. Landmark studies, systematic reviews, meta-analyses and large cohort studies were prioritised. Chronic immune activation and inflammation ("inflammaging"), immunosenescence, and the cumulative effects of ART and traditional risk factors drive accelerated and accentuated biological ageing in PLWH. This manifests as premature multimorbidity, an increased burden of cardiovascular disease, metabolic and bone disorders, HIV-associated neurocognitive disorder (HAND), non-AIDS-defining cancers, frailty, and geriatric syndromes. Polypharmacy and drug-drug interactions further complicate management, and traditional HIV services are poorly configured for these needs. Caring for the ageing HIV population requires a paradigm shift towards integrated, multidisciplinary and geriatric-informed models of care, systematic screening for comorbidity and frailty, structured medication review, and adoption of frameworks such as the WHO Integrated Care for Older People (ICOPE) approach. These changes should be urgently implemented in national HIV care systems, including Poland's.

Key words: HIV; ageing; multimorbidity; frailty; polypharmacy; HIV-associated neurocognitive disorder; models of care; comprehensive geriatric assessment.

1. Introduction

Since the acquired immunodeficiency syndrome (AIDS) was first described in 1981, more than 75 million people worldwide have been infected with the human immunodeficiency virus (HIV), and the virus continues to be transmitted, predominantly through sexual contact but also via mother-to-child transmission and exposure to contaminated needles [1]. The clinical course of untreated infection ranges from an acute retroviral syndrome through a prolonged asymptomatic phase to opportunistic infections and the dermatological, neuromuscular and systemic complications that define AIDS [1]. Early and accurate diagnosis - relying on fourth-generation serological assays and point-of-care testing - combined with combination antiretroviral therapy (ART), has fundamentally altered the natural history of the infection [1].

The consequence of this therapeutic success is profound: HIV infection has become a chronic, manageable condition, and the life expectancy of PLWH who are diagnosed early and treated effectively now approaches that of the general population. As a result, the HIV population is ageing rapidly. In many high-income settings, people aged 50 years and older already constitute the majority of PLWH, and the proportion continues to rise both because those infected in earlier decades are surviving into older age and because new diagnoses are increasingly made

later in life [2][3][4][5]. Modelled UNAIDS estimates indicate that HIV prevalence among adults aged 50 and above roughly doubled across successive age cohorts in the two decades following the mid-1990s [2].

This demographic transition creates challenges that neither classical infectious-disease medicine nor traditional geriatrics is designed to address. Older PLWH experience an excess burden of age-related conditions - cardiovascular disease, metabolic disorders, osteoporosis, neurocognitive impairment, and malignancy - that frequently appear earlier and cluster more densely than in age-matched HIV-negative individuals [6][7][8][9]. Superimposed on this multimorbidity are polypharmacy, a high risk of drug-drug interactions, frailty, and other geriatric syndromes. Meeting these needs demands a reorganisation of care towards integrated, multidisciplinary and geriatric-informed models.

Research objective. The aim of this review is to characterise the clinical and organisational challenges that arise at the intersection of HIV infection and ageing, and to summarise the evidence base for emerging models of integrated HIV-geriatric care.

Research problem. What are the principal clinical consequences of ageing in people living with HIV, and which models of care are best suited to address them?

2. Materials and Methods

2.1. Design and data sources

This is a narrative review. A structured search of the PubMed/MEDLINE database was performed for English-language articles, complemented by the current guidelines of the European AIDS Clinical Society (EACS) and the World Health Organization (WHO).

2.2. Search strategy and study selection

Search terms combined controlled vocabulary and free text relating to "HIV", "human immunodeficiency virus" and "antiretroviral therapy" with terms describing ageing and its clinical consequences: "ageing", "older adults", "multimorbidity", "inflammaging", "immunosenescence", "cardiovascular disease", "metabolic complications", "osteoporosis", "HIV-associated neurocognitive disorder", "non-AIDS-defining cancers", "polypharmacy", "drug-drug interactions", "frailty", "geriatric syndromes" and "models of care". Priority was given to landmark studies, systematic reviews, meta-analyses, large cohort studies and consensus guidelines, with an emphasis on publications from 2013 to 2026, while classical

foundational papers were retained where relevant. Reference lists of retrieved articles were screened to identify additional sources.

2.3. Data analysis

Owing to the narrative design, no formal quality-scoring instrument or quantitative synthesis was applied; the review aims to provide an integrated clinical and organisational overview rather than a pooled estimate of effect. Findings were organised thematically by disease domain and by model of care.

3. Results

3.1. Epidemiology of the ageing HIV population

The ageing of the HIV population is one of the most significant epidemiological shifts of the ART era. Analyses of UNAIDS estimates and survey data demonstrate a sustained, roughly two-fold increase in HIV prevalence among people aged 50 and over since the mid-1990s, with approximately 4.2 million people in this age group living with HIV globally by 2013 [2]. Both modelled estimates and cross-sectional survey data converge on the same conclusion: surveillance systems and services must adapt to a population that is growing older [2].

This trend reflects two complementary dynamics. First, effective ART allows people diagnosed in earlier decades to survive into their sixth, seventh and eighth decades. Second, a substantial and increasing proportion of new diagnoses occur in older adults; United States surveillance data for 2007 already indicated that roughly one in six new HIV diagnoses (16.8%) arose in adults over the age of 50 [5]. A systematic review and meta-analysis found that nearly half of newly diagnosed infections in the United States now occur in people over 50, and that diagnosis and treatment in older adults are systematically delayed by clinical misconceptions and overlapping comorbidities [3].

Older adults are especially vulnerable to late or missed diagnosis because both patients and clinicians frequently underestimate the risk of HIV acquisition in later life [5]. Late diagnosis has direct clinical consequences: delayed presentation is associated with lower CD4 nadir (the lowest recorded CD4+ T-lymphocyte count, reflecting the greatest degree of immune depletion), greater immune damage and a higher subsequent burden of age-related disease. Reviews of local and global demographic data emphasise that older PLWH are under-represented in prevention campaigns, epidemiological surveillance and clinical trials, leaving

important evidence gaps [4]. As the population continues to age, cardiovascular disease, osteoporosis and dementia are becoming defining features of the HIV clinic, requiring the collaboration of infectious-disease specialists and geriatricians [5].

3.2. Accelerated and accentuated ageing: inflammaging and immunosenescence

A central theme in understanding the ageing HIV population is that chronological age alone does not explain the excess burden of disease. Even with durable virological suppression, PLWH exhibit residual chronic immune activation and inflammation collectively termed "inflammaging" accompanied by premature immunosenescence (the age-related decline in immune function) [6][7]. These processes are thought to accelerate biological ageing, such that a person living with HIV may be biologically several years older than their chronological age.

In a cohort of 828 virologically suppressed adults, higher cellular immune activation was independently associated with the presence of multimorbidity and with the risk of new age-related conditions, while soluble tumour-necrosis-factor receptor I predicted mortality - supporting the concept that chronic inflammation and immunosenescence, rather than age alone, drive multimorbidity in PLWH [6]. Reviews of HIV as a chronic condition similarly conclude that it is associated with chronic inflammation and accelerated immunosenescence, which manifest clinically as an earlier onset and higher prevalence of age-related diseases and frailty than in the general population [7]. Because older PLWH are markedly heterogeneous, identifying those at greatest risk and offering an individualised, holistic and multidisciplinary approach is essential [7].

Even under effective ART, persisting immune dysregulation - marked by naive T-cell depletion and dysregulated cytokine secretion - raises the long-term risk of renal impairment, premature atherosclerosis, insulin resistance and metabolic bone disease [8]. Comprehensive reviews of ageing with HIV increasingly focus on biomarkers of accelerated biological ageing, including epigenetic "ageing clocks" (biomarkers that estimate biological age from DNA methylation patterns), which may allow earlier identification and monitoring of individuals at risk of age-related disease [9]. The distinction between "accelerated" ageing (the same diseases occurring earlier) and "accentuated" ageing (a higher prevalence at any given age) remains an area of active investigation, but both concepts underscore the need for proactive screening rather than reactive treatment.

3.3. Multimorbidity and cardiovascular disease

3.3.1. The multimorbidity burden

Multimorbidity, the co-occurrence of two or more chronic conditions, is the defining clinical challenge of the ageing HIV population. Age-related comorbidities cluster earlier and more densely in PLWH, and markers of immune activation, senescence and inflammation are independently associated with both the presence of multimorbidity and incident age-related disease [6]. The clinical implication is that older PLWH should be viewed not merely as patients with a single infection, but as complex, multimorbid individuals requiring coordinated management [7].

3.3.2. Cardiovascular disease

Cardiovascular disease (CVD) is now one of the leading causes of death among PLWH in the ART era [10][11]. The pathophysiology is multifactorial: HIV proteins such as Tat, Nef and gp120 accelerate atherosclerosis through direct and indirect mechanisms including endothelial dysfunction, chronic inflammation, immune activation and metabolic disturbance [10]. ART, while primarily life-prolonging, also contributes to the rising prevalence of chronic conditions such as CVD [10].

Cross-sectional studies of adults aged 50 and older confirm a higher prevalence of subclinical atherosclerosis in PLWH than in HIV-negative controls [12]. Importantly, cardiovascular risk in people ageing with HIV is driven by both traditional factors (age, smoking, hypertension) and HIV-specific factors such as duration of ART exposure and CD4 nadir [13]. Consequently, cardiovascular risk-assessment tools derived from the general population may underestimate true risk in PLWH, and assessment must incorporate HIV-specific variables rather than relying solely on standard scores [13]. The combination of traditional risk factors with the pathophysiological effects of HIV and ART substantially elevates cardiovascular risk, demanding multidisciplinary management and familiarity with complex therapeutic options [11].

3.4. Metabolic, skeletal and renal complications

As PLWH live longer on effective ART, recognition of the metabolic complications of chronic infection - dyslipidaemia, diabetes mellitus, osteoporosis and cardiovascular disease - has grown [14]. These complications arise both from HIV infection itself and, paradoxically, from

the otherwise highly effective antiretroviral treatment [14]. Because most are modifiable or preventable, active surveillance and screening are warranted [14].

A landmark analysis described a paradigm shift in HIV care from the treatment of opportunistic infections to the management of metabolic complications - lipodystrophy, dyslipidaemia and insulin resistance - affecting a large proportion of patients on combination therapy; it coined the phrase "the price of success" to capture the long-term metabolic cost of treatment [15]. Practical clinical reviews for primary-care physicians describe the core metabolic comorbidities of the ART era - dyslipidaemia, fat redistribution (lipodystrophy), insulin resistance and diabetes, and reduced bone mineral density - together with screening algorithms and management strategies [16]. Regular monitoring of metabolic parameters and cardiovascular risk is a recurring recommendation across this literature [16]. Reduced bone mineral density and osteoporosis warrant particular attention in older PLWH because they compound the risk of falls and fractures already associated with frailty and geriatric syndromes.

3.5. HIV-associated neurocognitive disorder in older adults

Despite virological control, HIV-associated neurocognitive disorder (HAND) remains a common complication in PLWH; the epidemiological pattern has shifted, with frank dementia now less frequent but milder forms of neurocognitive impairment predominating [17]. People aged 50 and over represent the fastest-growing segment of the HIV population; within this group, the prevalence of HAND has not fallen, and may have risen, with more severe cognitive deficits observed in older patients [18].

The pathogenesis of HAND in the ART era is multifactorial, encompassing central-nervous-system injury sustained before treatment, chronic immune activation, potential neurotoxicity of antiretroviral agents and age-related comorbidities such as cardiovascular disease and diabetes [17]. As the HIV population ages, the boundary between HAND and neurodegenerative dementias - particularly Alzheimer’s disease - becomes increasingly blurred [17][19]. A longitudinal study comparing older adults with HAND, patients with mild cognitive impairment due to early Alzheimer’s disease, and healthy controls found that hippocampal volume distinguished the two disorders, HAND being characterised by greater frontal and cerebellar atrophy, and early Alzheimer’s disease by more pronounced language and memory impairment [20]. These findings highlight the need for validated neuroimaging and neuropsychological biomarkers to differentiate HAND from early Alzheimer’s disease in older PLWH [19][20].

3.6. Malignancies: from AIDS-defining to non-AIDS-defining cancers

The epidemiology of cancer in PLWH has changed dramatically. In countries with wide ART coverage, the incidence of the three classic AIDS-defining malignancies - Kaposi sarcoma, non-Hodgkin lymphoma and cervical cancer - has dropped substantially, yet the risk remains disproportionately elevated, at approximately 800, 10 and 4 times the rates seen in HIV-negative individuals, respectively [21]. At the same time, non-AIDS-defining cancers (NADC) have become a growing source of morbidity and mortality [21][22].

The burden of common age-related, non-virus-associated cancers - for example, prostate and lung cancer - now exceeds that of virus-associated cancers among PLWH; ageing, behavioural factors and HIV-specific biological mechanisms jointly shape the incidence and outcomes of NADC [22]. A retrospective cohort followed over 28 years documented a dramatic decline in AIDS-defining cancers alongside a rising prevalence and incidence of NADC, driven by the ageing of the population and persistent inflammation [23]. Comprehensive reviews confirm that NADC are a significant cause of morbidity and mortality in the ageing HIV-positive population, with elevated incidence rates compared with the general population [24]. This shifting landscape mandates a reorientation of cancer screening and prevention programmes away from AIDS-defining cancers and towards the age-related, non-AIDS-defining cancers that now predominate [22][23].

3.7. Polypharmacy and drug–drug interactions

The accumulation of multiple chronic conditions inevitably leads to polypharmacy. An older person with HIV typically takes antiretroviral drugs alongside multiple medications for comorbid cardiovascular, metabolic, skeletal and geriatric conditions; the prevalence of polypharmacy rises with age and multimorbidity, frequently exceeding 50% in older PLWH [25]. As life expectancy improves, the risks of multimorbidity, polypharmacy and harmful drug interactions increase in parallel [26].

Older adults are more susceptible to drug interactions and adverse effects because of the pharmacokinetic changes that accompany ageing [26]. An early cross-sectional analysis of the HIV Outpatient Study demonstrated that both the extent of polypharmacy and the risk of interactions between antiretroviral and non-antiretroviral drugs increased with age, and it was among the first to document the scale of the problem systematically [27]. In a Spanish study of HIV-positive patients aged 65 and over, the prevalence of polypharmacy (five or more

medications) and of potential drug interactions was high, with age, number of comorbidities and number of medications being the principal risk factors [28].

Certain antiretroviral classes - notably protease inhibitors, the pharmacokinetic booster cobicistat (a CYP3A inhibitor used to enhance drug levels rather than an antiretroviral in its own right), and the older non-nucleoside reverse transcriptase inhibitor efavirenz - carry a particularly high risk of interaction with cardiovascular, lipid-lowering and central-nervous-system medications [26]. A comprehensive review of polypharmacy management in PLWH described its prevalence, associated factors, effects on ART outcomes and on nutritional and geriatric status, and the available interventions, concluding that a structured approach including regular medication review is a key element of care [25]. Six years' experience of a dedicated multidisciplinary outpatient clinic demonstrated that regular medication review involving a clinician, a pharmacist and an interaction specialist significantly improved treatment safety and may serve as a model for other centres caring for ageing PLWH [29].

3.8. Frailty and geriatric syndromes

Frailty, a state of increased vulnerability to stressors resulting from cumulative decline across multiple physiological systems, is a central concept in the care of older PLWH. Foundational cohort work using a frailty index (a validated cumulative-deficit measure) demonstrated that PLWH have a higher frailty burden than HIV-negative individuals of the same age - with greater severity among those with a lower CD4 nadir and longer duration of infection - and that frailty emerges as much as a decade earlier than in the general population [30].

A systematic review and meta-analysis of studies in PLWH aged 50 and over estimated a pooled prevalence of frailty of approximately 11% and of pre-frailty of approximately 47%; both figures are higher than in the general population and occur at younger ages, implying a need for routine geriatric assessment [31]. Earlier systematic reviews using the Fried phenotype (a five-item physical frailty scale) similarly reported an elevated prevalence of frailty, with predictors including low CD4 nadir, longer duration of infection, low physical activity and depression [32]. Cross-sectional studies confirm both a high prevalence of frailty and poorer physical function, weaker grip strength, slower gait and lower physical activity, in older adults with HIV [33].

Frailty is more than a descriptive label; it carries prognostic weight. The multicentre FUNCFRAIL study demonstrated that frailty, the geriatric syndromes assessed in that cohort

(including depression, cognitive impairment, falls and malnutrition), and multimorbidity each had a negative effect on mortality and quality of life in older PLWH; of the three factors, frailty exerted the greatest adverse effect [34]. Frailty is also independently associated with a higher risk of HAND, suggesting that it may act as a biological link between immunosenescence and neurocognitive impairment and may serve as a screening marker for cognitive risk [35]. Contemporary cohort data from high-income settings, such as the Canadian CHANGE HIV cohort, reaffirm that a low CD4 nadir is a primary predictor of frailty, underscoring the long-term impact of early immunological damage and the importance of timely ART initiation [36]. Taken together, these findings support the routine incorporation of comprehensive geriatric assessment (CGA) into standard care [34].

3.9. Models of integrated HIV–geriatric care

The clinical challenges outlined above expose a structural problem: HIV services were designed for a younger population and are poorly configured to manage accelerated ageing, frailty and multimorbidity [37][38]. There is, as yet, no gold-standard model of care for older PLWH, but a scoping review has systematised existing approaches and identified the key components of effective models: multidisciplinary working, comprehensive geriatric assessment and the integration of infectious-disease and geriatric expertise [38].

Expert consensus from clinics in North America and the United Kingdom has described three broad models of geriatric consultation for PLWH: an outpatient consultation or referral pathway; an integrated HIV–geriatrics clinic; and dually trained specialists within a single centre. A patient-centred approach and interdisciplinary expertise were universally identified as the essential ingredients of success [39]. Qualitative evaluation of the Golden Compass programme at the University of California, San Francisco - which co-locates HIV, geriatric and cardiology expertise with pharmacy and social-work support - found that both patients and clinicians rated the service highly, attributing gains in function and well-being to its holistic, geriatric-informed approach, which in turn strengthened patients' trust in their care team [40]. Contemporary reviews of innovative models confirm that integrating the principles of geriatrics into HIV care yields promising results in patient satisfaction, detection of geriatric syndromes and quality of life, describing a spectrum of models from geriatric consultation to fully integrated HIV-geriatric clinics [37].

National and international guidance is beginning to reflect this shift. The 2017 Italian guidelines were a pioneering attempt to integrate HIV care with the principles of geriatrics, offering

recommendations on frailty assessment, comprehensive geriatric assessment and polypharmacy management, while noting that the principles and goals of ART initiation in older patients remain the same as in the general HIV population [41]. The framing of HIV as a model of accelerated and accentuated ageing has prompted calls for a new discipline of "geriatric HIV medicine", in which comprehensive geriatric assessment is held to be the only adequate approach to managing the multidimensional state of frailty in ageing PLWH [42][43]. More recently, the WHO Integrated Care for Older People (ICOPE) framework - which centres on intrinsic capacity (the composite of an individual's physical and mental capacities) and functional ability - has been proposed as a complement to standard HIV monitoring and as a tool for the early identification of individuals at risk of functional decline [44].

Authoritative guidelines increasingly incorporate the needs of older PLWH. The major revision of the EACS guidelines (version 13.0, 2025) is organised into a section on HIV management and prevention and a section on comorbidities and other clinical topics, with updated recommendations on switch strategies, prophylaxis, vaccination and the management of comorbidities in older PLWH; recommended first-line regimens include tenofovir (as TDF or TAF) with lamivudine or emtricitabine plus an integrase inhibitor (dolutegravir or bictegravir) or doravirine [45]. The WHO consolidated guidelines likewise emphasise the need to adapt health systems to a growing population of ageing PLWH requiring management of multimorbidity [46]. A key review published in JAMA argued that standard HIV regimens and guidelines are insufficient for ageing PLWH, and recommended the integration of geriatric assessment and multidisciplinary collaboration as the standard of care [47]. Cross-sectional evidence that a high proportion of older PLWH have at least one geriatric syndrome, more often than the general population, provides a clinical rationale for mandatory comprehensive geriatric assessment [48].

3.9.1. Practical elements of a geriatric-informed HIV service

Synthesising the evidence, several practical components recur across successful models of care for ageing PLWH:

- **Systematic comorbidity screening from age 50 -** routine assessment of cardiovascular risk (incorporating HIV-specific factors), metabolic parameters, bone mineral density, renal function, and age- and sex-appropriate cancer screening [13][14][16][22]

- **Frailty and functional assessment -** periodic evaluation using a validated frailty measure and elements of comprehensive geriatric assessment, given the prognostic weight of frailty for mortality and quality of life [31][34][48]

- **Cognitive screening -** structured evaluation for HAND with awareness of the overlap with neurodegenerative dementias in older adults [17][20]

- **Structured medication review -** regular review of the full medication list by a clinician–pharmacist team to identify and prevent clinically significant drug–drug interactions and inappropriate prescribing [25][29]

- **Multidisciplinary coordination -** close collaboration between infectious-disease specialists, geriatricians, cardiologists, pharmacists, mental-health professionals and social workers [39][40]

- **Adoption of validated frameworks -** use of the WHO ICOPE approach and the comorbidity recommendations of the current EACS guidelines to standardise care [44][45]

4. Discussion

The evidence reviewed here has direct implications for the organisation of HIV care in Poland and other Central-European settings. As the Polish HIV cohort ages, infectious-disease services will increasingly encounter patients with cardiovascular disease, metabolic disorders, neurocognitive impairment, malignancy, polypharmacy and frailty. Yet the models of care best suited to these needs, integrated HIV-geriatric clinics, comprehensive geriatric assessment and structured medication review, remain unevenly implemented. The international experience suggests several priorities: systematic screening for comorbidity and frailty from the age of 50; routine medication review to detect and prevent clinically significant drug-drug interactions; closer collaboration between infectious-disease specialists, geriatricians, cardiologists, pharmacists and mental-health professionals; and the adoption of frameworks such as WHO ICOPE and the comorbidity recommendations of the EACS guidelines [37][39][44][45]. Because no single model has been established as superior, local services can reasonably begin with the most feasible option - a geriatric consultation pathway - and progress towards fuller integration as capacity allows [39].

This review has limitations. It is a narrative rather than a systematic review, and much of the cited evidence derives from high-income settings that may differ from the Polish healthcare system in resources and organisational structure. The heterogeneity of the older HIV population, and the still-evolving distinction between accelerated and accentuated ageing, mean that individualised assessment remains essential. Nonetheless, the convergence of evidence across epidemiology, mechanism, comorbidity and health-services research points clearly towards the required direction of care.

5. Conclusions

Antiretroviral therapy has been so successful that the defining clinical challenge in HIV medicine is no longer the treatment of opportunistic infections but the management of an ageing, multimorbid population. Chronic inflammation and immunosenescence drive accelerated and accentuated biological ageing, producing an excess and early burden of cardiovascular, metabolic, neurocognitive and oncological disease, compounded by polypharmacy, frailty and geriatric syndromes [6][7][9]. Traditional HIV services are not configured for these needs.

Meeting the needs of the ageing HIV population requires a paradigm shift towards integrated, multidisciplinary and geriatric-informed care. The essential elements are clear: systematic screening for comorbidity and frailty, comprehensive geriatric assessment, structured medication review, and the adoption of validated frameworks such as WHO ICOPE and current EACS guidance [37][44][45][47]. Implementing these changes, including within the Polish healthcare system, is now an urgent priority if the therapeutic gains of the ART era are to translate into healthy, functional ageing for people living with HIV.

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AUTHORS'S CONTRIBUTION

Conceptualization: TK, PK, MK, KI, AG

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Software: TK, PK, GP, DG, AU

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Conflicts of Interest

The author(s) declare no conflict of interest.

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