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Development of The Johns Hopkins University School of Nursing Adult/ Geriatric Primary Care Nurse Practitioner Program in HIV Prevention, Treatment, and Care

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In response to the call to create an AIDS Education and Training Center for Nurse Practitioner Education by the Health Resources and Services Administration, The Johns Hopkins University School of Nursing embarked on a transformative curriculum overhaul to integrate HIV prevention, treatment, and care into the Adult/Geriatric Nurse Practitioner Program. A six-step process outlined in the Curriculum Development for Medical Education was followed. A pilot cohort of Adult/Geriatric Nurse Practitioner students were enrolled, including 50% primary care setting and 50% HIV-focused primary care through a 12-month HIV continuity clinic experience. Through this pilot, substantive changes to the program were adopted. Programmatic outcomes were not compromised with the modification in clinical hours. The model of a 12-month HIV continuity clinical experience reduced the number of required preceptors. This model has important implications for the HIV workforce by demonstrating successful integration of HIV and primary care training for nurse practitioners.

(Journal of the Association of Nurses in AIDS Care, 27, *223-233*)

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JOURNAL OF THE ASSOCIATION OF NURSES IN AIDS CARE, Vol. 27, No. 3, May/June 2016, 223-233
http://dx.doi.org/10.1016/j.jana.2015.12.006

Key words: *HIV, nurse practitioner, primary care, workforce*

Persons living with HIV (PLWH) deserve quality, patient-centered, and life-affirming care that is rooted in evidence. Poor access to such care may result in stigma, late diagnosis, opportunistic illnesses, and immunologic decline, including the potential development of AIDS. New infections continue to disproportionately impact underserved and marginalized populations, such as communities of color, persons with lower socioeconomic status, and persons engaged in substance use, as well as men who have sex with men and transgender women (Centers for Disease Control and Prevention [CDC], 2013, 2015). The National HIV/AIDS Strategy for the United States provides a roadmap to reduce new HIV infections, increase access to care, improve health outcomes, increase provider diversity, and reduce HIV-related disparities and health inequities. Notably, the plan calls for "developing models of competent care that treat the whole person, as well as the virus" (Office of National AIDS Policy, 2015. p. 5).

Baltimore, Maryland, and the District of Columbia in the United States are among the 12 metropolitan statistical areas most affected by HIV (Centers for Disease Control and Prevention, 2015). HIV care specialists and primary care clinicians are widely available in the urban areas of this region. However, the HIV specialist often becomes the default provider for primary care services due to overlapping needs for prevention and chronic disease management, and a lack of HIV expertise among primary care providers.

Nurse practitioners (NPs) are highly trained primary care providers with evidence demonstrating that health outcomes for PLWH under their care are comparable to those of physicians (Ding et al., 2008). A recent national HIV provider survey demonstrated that NPs, more than any other clinical group, reported greater attention to adherence and retention in care (Weiser et al., 2015). Patient satisfaction is often highly rated by patients who receive care from NPs (Swan, Ferguson, Chang, Larson, & Smaldone, 2015), and fewer health inequities have been demonstrated by providers with greater cultural competence (Saha et al., 2013). Despite these findings, training programs designed to integrate HIV clinical care competencies into primary care are lacking for the NP.

In response to the call to create an AIDS Education and Training Center for Nurse Practitioner Education by the Health Resources and Services Administration, The Johns Hopkins University School of Nursing (JHUSON) embarked on a transformative curriculum overhaul to integrate HIV prevention, treatment, and care into the Adult/Geriatric Nurse Practitioner (AGNP) Program. We will review the process of curriculum development, pilot implementation, and modification of the AGNP HIV-Primary Care Certificate (HIV-PCC) program, which was designed to enhance the development of the primary care workforce in caring for persons at risk for or living with HIV.

Methods

A six-step process outlined by Kern, Thomas, and Hughes (2009) was followed to facilitate an iterative curriculum design process that was grounded in the needs of the community as well as trainees within the institution (Figure 1). The evaluation proceeded in three phases using a continuous quality-improvement process that included: Phase I (developmental); Phase II (pilot); and Phase III (implementation).

In Phase I, a steering committee of five faculty and a senior AIDS Certified Registered Nurse with subject matter expertise was formed. The committee chose to encompass HIV care and HIV treatment as distinct entities in the program design. HIV care refers to the health system and clinical infrastructure that support client engagement, adherence, and retention, while HIV treatment focused on the use of antiretroviral therapy, management of opportunistic infections and co-infections, and the associated clinical aspects.

Step 1: Problem Identification and General Needs Assessment

The steering committee began by conducting an extensive literature review identifying the current epidemiologic profile within the greater Baltimore area and the State of Maryland, as well as national

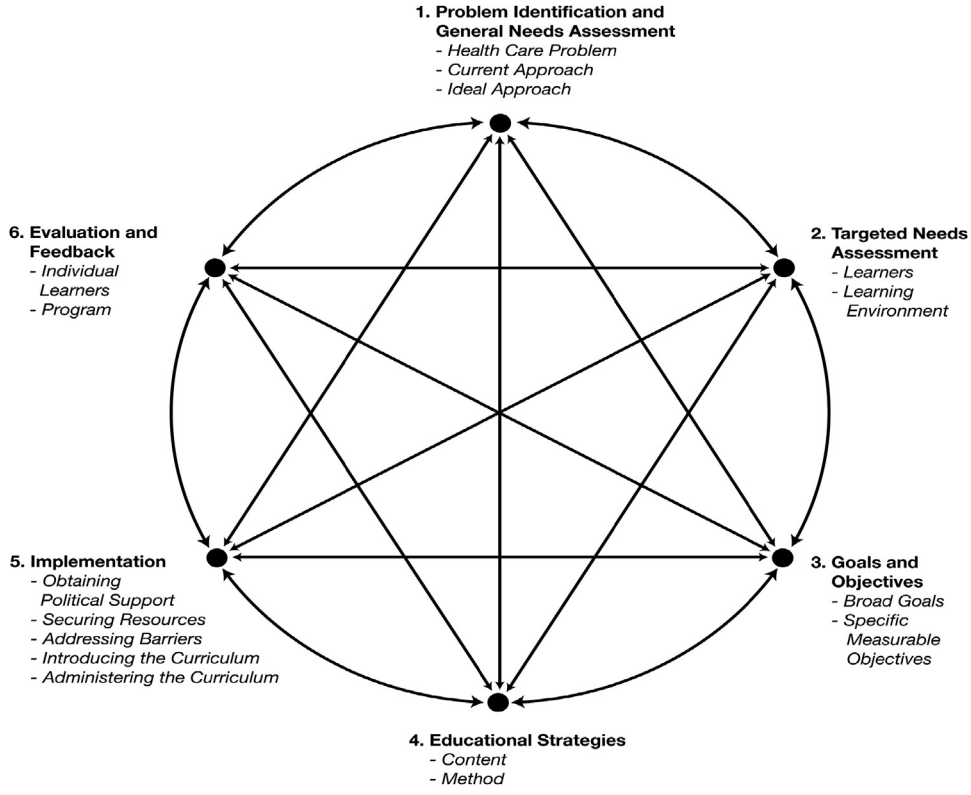

Figure 1. The Six-Step Curriculum Process Model. Reprinted with permission of The Johns Hopkins University Press from Kern, D. E., Thomas, P. A., & Hughes, M. T. (Eds.). (2009). *Curriculum development for medical education: A six step approach.* p. 6, Figure 1.1. Baltimore, MD: Johns Hopkins University Press.

trends in HIV treatment and care. The section below summarizes the overarching themes within the data at the time of program development, highlighting the critical need for such a program in this region.

- The Baltimore and Washington metropolitan areas are among the hardest hit by HIV in the United States (CDC, 2013; Maryland Department of Health and Mental Hygiene, 2012).
- Aging with HIV is a challenge for primary care management (Capeau, 2011; U.S. Department of Health And Human Services, 2013).
- Despite having a greater prevalence, communities of color and sexual minorities lack providers who reflect their race, sexual identity, and/or culture (Earl et al., 2013; Sabin, Riskind, & Nosek, 2015).
- Great strides have been made to reduce the incidence of infection in people who inject drugs, yet substance abuse remains a key challenge in primary care (Gonzalez, Barinas, & O'Cleirigh, 2011; Mimiaga et al., 2013).
- There is a substantial shortage of HIV primary care providers with specialized training in HIV treatment and care (U.S. Department of Health and Human Services, 2010).

Step 2: Targeted Training Needs Assessment

The steering committee reviewed the available data and sought to determine the level of preparation of the community of interest, the JHUSON student body. A seven-question, anonymous survey was developed and approved with exempt status by The Johns Hopkins University investigational review board. This surveymonkey.com link was e-mailed to all JHUSON students (n = 802), with weekly reminders between February and March 2013.

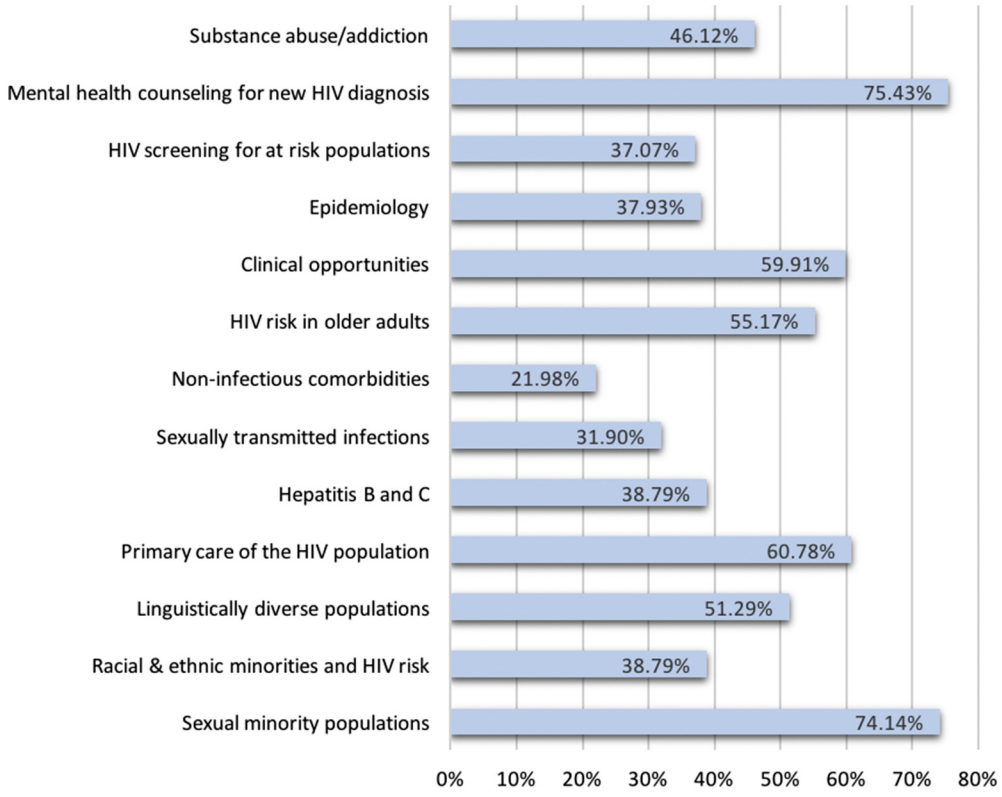

Figure 2. Johns Hopkins University School of Nursing curriculum survey student training needs assessment.

A total of 232 responses (28.9%) were received: 92% female and 78.3% Caucasian, 11.7% Asian, and 9.1% African American, with 3.9% reporting Hispanic ethnicity. Of the respondents, 75.2% reported being unprepared at present to provide HIV and primary care services. Students were asked to comment on specific areas they believed were insufficient in the education program. The majority (>50%) felt their preparation was lacking in the following critical areas: counseling for newly diagnosed patients, HIV screening in at-risk populations, caring for sexual minority communities, caring for linguistically diverse communities, primary care in HIV, HIV and older adults, and clinical opportunities with PLWH (Figure 2).

Step 3: Determine Goals and Objectives

The data led the steering committee to critically reflect on the then-current training model and challenged the assumption that entry-level HIV content was adequately addressed in the course of study. As a result, a key programmatic objective became the development of an HIV competency roadmap to address: (a) the entry-level competencies of care, treatment, and prevention of HIV; and (b) the associated didactic and clinical coursework that facilitated mastery of these competencies. The roadmap made it clear that modification of existing AGNP courses along with the development of three new HIV-content-focused courses was required to address the required competencies. These curriculum enhancements were designed to transform the curriculum into an integrated HIV primary care program.

Performance-related goals were designed to measure overall programmatic outcomes to track this transformative curriculum change. Outcomes are evaluated at several points: (a) successful completion of required courses within the prescribed time-frame, (b) clinical and cultural competency progression by preceptor assessment, (c) percentage of students completing the degree, (d) percentage graduating

within the prescribed time frame, and (e) the percentage of students who successfully pass the professional examination (i.e., AGNP Certification Exam) on the first attempt. Completion and pass rate of the Advanced AIDS Certified Registered Nurse (AACRN) examination was determined to be the final measure of program outcome.

Step 4: Education Strategies

Upon initiating curriculum enhancement, the original AGNP program was a 40-credit, 18-month program of study that prepared graduates to provide person-centered, evidence-based primary care. The program had 548 clinical hours and was based on the Consensus Model for Advanced Practice Registered Nurse Regulation (APRN Consensus Work Group & National Council of State Boards of Nursing APRN Advisory Committee, 2008), the Criteria for Evaluation of Nurse Practitioner Programs (National Task Force on Quality Nurse Practitioner Education, 2012), the NP Core Competencies with Curriculum Content (National Organization of Nurse Practitioner Faculties, 2012), and the Adult/Gerontology Primary Care Nurse Practitioner Competencies (American Colleges of Nursing, 2010).

As developed for pilot implementation, the enhanced AGNP with HIV-PCC is a 52-credit, 660-clinical-hour, 18-month, fulltime course of study with 50% of the primary care training occurring in an HIV care setting (Table 1). The HIV-PCC program includes 12 credits across five required core courses and 112 additional clinical hours in specialty rotations. Students are required, under the supervision of their preceptors, to manage a panel of 30 patients (i.e., panel management) during a 12-month period. Faculty felt that the most effective strategy for providing competency for comprehensive HIV treatment and care was to facilitate experiential learning in HIV primary care settings. In this practicum, the learner spends 1 day a week (10-12 hours) in the HIV primary care clinic over a 12-month period.

A substantial change to the existing AGNP program was required to integrate HIV-PCC didactic and clinical content. This transformative model replaced the AGNP clinical rotations, which traditionally rotated to a new site each semester, with 12-month continuity clinic experiences in a single HIV primary care site. The intent of this change was to allow students greater time for self-assessments and personal audits of their own patient care and clinical practice. To directly facilitate this process, an additional course was designed and placed in the student's last semester of study. The purpose of this course is to support individual and peer-driven critical appraisal and synthesis of clinical care by addressing three key questions: (a) Who in my patient panel has an undetectable viral load and why?; (b) Who in my patient panel has a detectable viral load and why?; and (c) Have I optimized both HIV and primary care clinical outcomes in my patients? The course further integrates key clinical indicators of quality of care while challenging students to consider barriers. Such an experience affords the student the opportunity to improve their own care cascade and enhance clinical decision-making in a patient-centered manner.

Step 5: Implementation

Transition from Phase I to Phase II (Pilot) occurred after a draft curriculum was designed and approved for implementation. In preparing to implement this program, the steering committee had to address important barriers and obtain necessary regulatory approvals to ensure that accreditation standards were met.

Overcoming barriers. Once clinical sites were identified, the potential for a reduction in clinical productivity (i.e., lower billed revenue) by precepting providers became the largest barrier to implementation. A comprehensive review of The Johns Hopkins University School of Medicine approach for medical education and other nursing programs that use a compensation-based preceptor model was completed. To overcome this barrier, the steering committee decided to compensate preceptors for the potential loss of billed revenue by providing 5% effort to the preceptor for each student.

Academic and regulatory approvals. Prior to implementing any new academic program at JHUSON, a series of approvals must occur in the institution and with external regulatory agencies. Given that HIV-

Table 1. HIV-PCC Enhancement of Johns Hopkins University School of Nursing Adult/Geriatric Nurse Practitioner Program (in bold)

Semester	Courses	Credits	Adult/Geriatric Nurse Practitioner HIV Primary Care Provider	
Fall	Clinical Pharmacology	3	In addition to an orientation to HIV-PCC	
	Physiology/Pathophysiology	3	program, students in this semester gain	
	Advanced Health Assessment and Measurement	2	fundamental building blocks for primary	
	Advanced Health Assessment Adult/Geriatric Variation	1	care practice	
	Diagnosis, Symptom, and Illness Management I	2	No changes or modifications are expected in this semester of study	
Winter	**Diagnosis, Care and Management of Persons with HIV/AIDS**	3	Students will complete a rotation in Prevention Clinical Sites	
	HIV and Comorbidities Health Assessment Clinical	1	Health Assessment with Exemplar HIV-infected Patients (HCV, HBV, Substance abuse, Older adults) 56 clinical hours	
Spring	Human and Family Development - Lifespan	2	Clinical Day 1 274 clinical hours	Clinical Day 2 274 clinical hours
	Diagnosis, Symptom, and Illness Management II	2	**Adult/Geriatric HIV**	Adult/Geriatric General
	Advanced Practice in Primary Care I	4	**Primary Care**	Primary Care Clinic
	Statistical Literacy and Reasoning in Nursing Research	3		Rotation #1
	Health Promotion, Disease Prevention	2		
Summer	Advanced Practice in Adult Primary Care II	3		Adult/Geriatric General
	Applications of Research to Practice	3		Primary Care Clinic
	Health Disparities	3		Rotation #2
Fall	Philosophical, Theoretical, and Ethical Basis for Nursing	3		Adult/Geriatric General
	Advanced Practice nursing: Clinical Topics and Professional Issues	4		Primary Care Clinic Rotation #3
	Context of Healthcare for Advanced Practice Nursing	3		
	HIV Complex Continuity Care	3	**HIV Comorbidity Specialty Rotations 56 clinical hours**	

Note. HIV-PCC = HIV Primary Care Certificate; HBV = hepatitis B virus; HCV = hepatitis C virus.

PCC sits within and requires enhancements to an existing and previously approved AGNP program of study, the approval process began with the Master's curriculum committee and proceeded through the institution-specific review process. Once all internal clearances were granted, a submission was required to the Maryland Higher Education Commission for statewide approval and accreditation.

Examination of entry-level advanced practice nursing competency. The steering committee felt it was essential that the programmatic enhancements did not negatively impact preparation for the American Nurses Credentialing Center or American Academy of Nurse Practitioners certification examinations. As the program was the first for NP education, the steering committee also sought to recognize the exceptional efforts students put forth to gain content-level expertise. The program sought curriculum review by the HIV Nursing Certification Board and it was determined to meet the minimal education requirements to allow students to sit for the AACRN examination directly upon completion of their degree. This closed-book examination provided a comprehensive assessment of our students' knowledge on entry into practice. In preparation for this examination, students received a comprehensive 8-hour preparatory review course. They were also given details about sitting for additional interprofessional HIV

specialty certification once the necessary number of practice hours were fulfilled.

Step 6: Evaluation and Feedback

The evaluation approach for our curriculum enhancement began with the creation of a rapid-cycle, continuous quality-improvement process. Three separate phases were developed to separate the targeted outcomes for each phase of the work, which allowed for short-term goal identification and immediate feedback into curriculum improvements through the design and the pilot implementation. The results of the pilot curriculum implementation led to the findings and changes summarized below.

As part of the evaluation process, pilot students were requested to provide ongoing feedback. Each student met individually with faculty and staff throughout the program to review progress and need for additional supportive infrastructure. Students kept a reflective journal of their clinical experiences and were specifically asked to detail their own views about their growth. Finally, the evaluation coordinator for the grant met with the students each month for the first three sessions of the pilot project and quarterly thereafter for the purpose of debriefing, discussing concerns, and facilitating collaborative learning approaches to clinical challenges.

Results

Pilot Implementation

The program began with four students in September 2013, as outlined in the Pilot Curriculum in Table 2. In total, 96 patients received care during the 12-month continuity clinic, with an average of 24 patients having at least two visits per student. Patients were predominantly African American (96%) and female (56%), with a mean age of 50.5 years. The student panels also included 16% sexual minority, 23% past/current substance users, and 40% hepatitis C co-infection. The median CD4+ T cell count at baseline was 527.5 cells/mm^3 (range 452-713 cells/mm^3), with the majority (86%) on antiretroviral therapy with an undetectable viral load.

The evaluation and feedback made by pilot students resulted in substantive changes to the program noted in the Final Curriculum. These changes included (a) reordering of the didactic coursework to facilitate mastery of health disparities content earlier in the program; (b) increasing the total number of AGNP clinical hours for both HIV and primary care; (c) adding an optional hepatitis C specialty certification in collaboration with the Johns Hopkins University School of Medicine; (d) increasing content hours in sexually transmitted infections, including a standardized patient model for screening; (e) increasing experiential learning opportunities; (f) increasing evaluation sessions from quarterly to monthly; and (g) adding a 1-day AACRN test preparation review at the end of the program.

All four students successfully completed the program in the specified time frame and were able to meet the standards set forth for this academic and clinically rigorous program. The pilot program outcomes included a 100% pass rate for the American Nurses Credentialing Center national AGNP certification examination. All pilot students found a career path in a primary care setting with individuals at risk or living with HIV and/or associated co-infections. The AACRN test review has been launched with students planning to sit for this examination within the first year of program completion.

Benefits of Integration of the HIV-PCC Program within the AGNP Program

The integration of the HIV-PCC program addresses key populations impacted by HIV in Maryland while maintaining the existing length of the program and ensuring alignment with national accreditation standards. This all occurred within the context of maintaining the costs of tuition in comparison to a stand-alone program. The design of the program also reduced the total number of clinical preceptors required per student from six (two per semester for three clinical semesters) to four (one HIV continuity clinical preceptor for 12 months and one primary care preceptor for three clinical semesters). For our pilot, this meant the school required eight fewer preceptors for the year for students in the program.

Table 2. Comparison of Pilot and Final Curricula

Original Didactic Curriculum	Pilot Curriculum	Final Curriculum
	Standard AGNP Program Curriculum with didactic additions, in this order: - HIV Diagnosis, Care, and Management (3 credits) - HIV Health Assessment and Diagnostic Reasoning (1 credit) - Health disparities (3 credits) - HIV Complex Continuity Care (3 credits)	Enhanced AGNP Program Curriculum, with new order: - Health disparities (3 credits) - HIV Diagnosis, Care, and Management (3 credits) - HIV Health Assessment and Diagnostic Reasoning (1 credit) - Health Promotion/Disease Prevention (2 credits with HIV experiential learning opportunities) - HIV Complex Continuity Care (3 credits)
Primary Care Clinical (50% of clinical hours)	274 clinical hours with rotations changing each semester	320 clinical hours with clinical location changing each semester
HIV Primary Care Clinical (50% of clinical hours)	12-month continuity clinic managing a panel of 30 patients; 274 clinical hours minimum	12-month continuity clinic managing a panel of 30 patients; 320 clinical hours minimum
Specialty Care Clinical within the HIV Complex Continuity Course	56 hours of specialty rotations	56 hours of specialty rotations HCV Certificate Program with SOM (12 months)–includes online case studies and 4 clinical sessions STI Clinical Training Workshop
Experiential learning opportunities within the Health Promotion/ Disease Prevention Course (Example opportunities shown)	Transgendered Action Group street outreach with sex workers	- Transgendered Action Group street outreach and harm reduction brochure - HCV Patient Education brochure for the Johns Hopkins University Center for Viral Hepatitis - Web site development for PrEP for The Johns Hopkins University REACH HIV Nursing Institute
Debrief and Evaluation Frequency	Quarterly debrief sessions with evaluation team Quarterly evaluation meetings with faculty	Monthly debrief sessions with evaluation team Quarterly evaluation meetings with faculty
Program outcome	Completion of AACRN Examination	1-day AACRN examination preparation course; Completion of AACRN examination upon graduation

Note. AGNP = Adult-Geriatric Nurse Practitioner; HCV = hepatitis C virus; SOM = School of Medicine; STI = sexually transmitted infections; PrEP = pre-exposure prophylaxis; REACH = Research, Education, Advocacy, Community, Health; AACRN = Advanced AIDS Certified Registered Nurse.

Preceptor Patient Schedule

During the first semester of the program it was necessary to schedule patients seen with the student in 1-hour intervals. This reduced the providers' patient schedule by 50% for that clinical session during the spring semester. The students transitioned by the end of the first semester to either 15- or 30-minute scheduled appointments consistent with their respective clinical site's standard patient visit time.

Discussion

Our program provides the first evidence of an HIV primary care training in-service model for the NP. The National HIV/AIDS Strategy for the United States notes,

> Meaningful improvements in health outcomes require adoption of policies that will produce a diverse workforce large enough to care for all PLWH and at risk for HIV and that has the appropriate training and technical expertise to provide high-quality care consistent with the latest prevention and treatment guidelines. (Office of National AIDS Policy, 2015, p. 33)

In order to increase access to care and improve health outcomes for PLWH, education programs must keep pace with the clinical arena. Nursing faculty must encourage curriculum innovations that facilitate integration of primary and HIV treatment and care. The HIV-PCC program is a model of curriculum innovation that affords students the opportunity to work with key populations impacted by HIV in the region. The program provides students with state-of-the-science content and places them in a uniquely blended approach of HIV treatment and care within the AGNP training program. The experience prepares students for the complicated nature of engagement and retention in HIV primary care. The longitudinal nature of the program allows them to actively participate in methods to support adherence, engagement, and retention in care with a patient panel.

The focus of our curriculum on both the human elements of HIV disease along with the clinical aspects of management is preparing students for what the National Strategy calls, "models of competent care that treat the whole person, as well as the virus" (Office of National AIDS Policy, 2015, p. 5). The 12-month continuity clinic experience also affords students the opportunity to reflect and evaluate the impact of clinical, mental health, psychosocial, and other factors on patient engagement and retention in HIV care. This is a stark contrast to the baseline experience at our institution that included the potential for a semester-long HIV rotation in which the student might engage with a patient only during a single encounter.

Boehler and colleagues (2015) described an in-service training model for primary care providers that included 20 hours of HIV didactic training coupled with 12 hours of clinical mentoring, which occurred over a 12-month period. The authors noted improvements in clinical competency across multiple domains. While our sample size during the pilot did not allow evaluation of pre-post competency improvement, the pilot evaluation suggested that the implementation of the present model, with 50% dedicated HIV continuity of care, did not adversely impact completion of the national AGNP certification examination. Student continuity clinic patient profiles reflected the epidemiologic profile of HIV in the region and conformed to learner-identified priorities to improve deficiencies in the AGNP primary care curriculum. Student participation and feedback was critical to move the pilot program into the final curriculum model, including the identification of supplemental training needs based on continuity clinical experiences. As NPs continue to provide increasing primary care services on par with other providers (Ding et al., 2008), integrated training models for HIV primary care are required to meet the needs of the HIV health workforce (U.S. Department of Health and Human Services, 2013). This training approach appears to fill this important need.

Limitations

While the pilot evaluation of our program resulted in significant curriculum improvements, the pilot group was limited, including only four students. We were not able to directly measure patient satisfaction and/or perceived cultural competence within the continuity clinical sessions. This would have provided greater understanding of the progam's ability to facilitate these aspects of care, both of which are associated with engagement and retention in care. Our program included financial support of 5% effort for participating preceptors as a result of grant funding. While costs may vary, our standard allocation for 5% effort on a median salary of $102,500 including necessary fringe benefits of 34.5% (total salary + benefits of $137,863) would be $6,933.13 per preceptor per year, based on the current preceptor salary mix. Once funding is no longer available, the costs of preceptor participation may not be sustainable and the

program will likely have to pass these costs on to students. The program reduced the required number of clinical preceptors, thereby decreasing the effort of the program to obtain these vital human resources, which may help offset student costs associated with the program in the future. Importantly, there were no additional costs in this model associated with the required elective didactic coursework.

Conclusions

We reviewed the development of an integrated HIV primary care certificate program. Our model has important implications for training the HIV workforce by demonstrating successful integration of HIV and primary care training for NPs. Graduates of the pilot program were well prepared for the current realities of primary care and, as such, were highly employable, with job offers both locally and nationally. Further evaluation is needed to determine if the success of the pilot implementation will continue with scale-up of the program.

Disclosures

The authors report no real or perceived vested interests that relate to this article that could be construed as a conflict of interest.

Key Considerations

- Nurse practitioners are highly trained primary care providers, with evidence demonstrating that health outcomes for persons living with HIV under their care are comparable to those for patients under physicians' care.
- Despite this, options for training programs designed to integrate HIV clinical care competencies into primary care are limited for nurse practitioners.
- An HIV specialization program integrated into an adult-geriatric nurse practitioner program is a feasible option to increase graduates' abilities to provide care to patients living with HIV infection.

Acknowledgments

A special thank you to the pioneering pilot cohort for their dedication to making this program a success. The authors would like to thank Paul Sacamano, ANP-BC, ACRN, for his assistance with preparing this manuscript. The AIDS Education and Training Center for Nurse Practitioner Education at Johns Hopkins University School of Nursing is funded under HRSA grant # 1 H4AHA26220-02-00.

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IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Geriatric-HIV Medicine Is Born

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(See the Review Article by Singh et al on pages 501–6.)

Keywords. geriatric; HIV; aging; geriatric care.

Ten years ago, the first modeling studies showed that the life expectancy of people living with human immunodeficiency virus (HIV) who demonstrated good immunological recovery is close to that of the general population [1]. Now we know that aging with HIV is a fact of life. With this realization has come a move to understand healthy life expectancy in people living with HIV. In this effort, the remarkable progress in HIV/AIDS medicine can benefit from what has been learned in geriatric medicine. Over many decades, geriatrics has developed clinical principles and practices that, in their focus on function (and not just disease), aim to enhance the quality of life of elderly people.

In this issue of *Clinical Infectious Diseases*, a review by Singh and coauthors celebrates the birth of "geriatric-HIV medicine." They forecast how it can rapidly catch up with related medical specialties, such as "ortho-geriatrics" [2], "cardio-geriatrics" [3], or "onco-geriatrics" [4]. The prerequisite for geriatric medicine and HIV medicine to interact is that they share some basic geriatric nomenclature. This is not an option: by speaking the same language, we can share principles and tools.

Some concepts are key. First, as they point out, there is more to understanding the complexity of health in aging than assessing noninfectious comorbidities and multimorbidity. Another centerpiece of the argument is that as people with HIV infection live longer, many are developing conditions and syndromes that are common in older adults but are only loosely related to disease counts. Two people with the exact same comorbid conditions can have very different functional aging trajectories; in contrast, the degree of frailty provides a reliable prognostic guide, something seen in many settings, and across the life course [5–8]. This also appears to hold in HIV [9]. The transition from evaluating comorbidities in HIV to implementing comprehensive geriatric assessment requires both structural and cultural changes in patient evaluation. Such changes will gain by understanding frailty [10, 11]. As a measure of biological age, frailty, better than chronological age, can describe both a health state and a geriatric syndrome. Frailty, more than multimorbidity, allows us to grasp the complexity of age-related pathophysiologic changes and does so in ways that can alert us to effective clinical interventions [12].

GERIATRICIANS IN HIV CLINICS?

Singh and colleagues examine several geriatric consultation models: referral to a geriatric clinic, assessment within a PLWH practice, and/or assessment in home. We do not yet know which is the most effective combination of resources, but whatever is available should be explored. We will need to learn how to screen for frailty, how to assess and treat common geriatric syndromes such as delirium, impaired mobility, falls, and polypharmacy. Some of this will require adaptation of what otherwise happens in aging. For example, will there be more specific pathways to delirium reflecting specific neurological consequences of HIV or of the medications used in its treatment? Likewise, tools that have worked well in geriatric assessment may need to be adapted to the assessment of HIV-infected persons. Vulnerabilities for disability and obstacles to care that are HIV-specific must also be taken into consideration, including social vulnerability and interaction between HIV and aging stigma. Each of these questions can help make up a rich and important research agenda, likely to advance disciplines in both care of older adults and persons living with HIV.

OPPORTUNITIES FOR INNOVATION IN CARE OF PEOPLE WITH COMPLEX NEEDS

Given the shortage even now of geriatricians in many developed countries, although some centers may lead in developing a needed Geriatric-HIV Medicine academic core, most HIV clinics wishing to incorporate the lessons of geriatric medicine can expect to add to their current offerings what works well in the assessment of aging people in general. Such work should be undertaken in the spirit that it can inform more generally

Received 20 March 2017; editorial decision 25 March 2017; accepted 31 March 2017; published online April 6, 2017.

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Clinical Infectious Diseases® 2017;65(3):507–9

DOI: 10.1093/cid/cix316

the care of people with complex needs, especially as they age [13, 14]. Further, we need not repeat their more painful lessons to learning from geriatricians. For example, confusion arises from the variable meanings of the term "comprehensive geriatric assessment." In the United Kingdom in particular, it is understood to also incorporate management and not just evaluation. In contrast, in many North American context geriatric assessment can be synonymous with mere risk stratification—reflecting an assumption (of people unaware of the active and evolving evidence base for its effectiveness) [15–17] that there is little to be done for frail patients other than to "place" them appropriately (eg, by assigning them to the correct level of long-term care). Similarly, as with other cognitive (as opposed to procedure-based) specialities, physician costs historically have been inadequately captured in the fee-for-service environment. Singh et al. note the increase in subspecialty consultation (eg, citing cardiology, nephrology, oncology) for people living with HIV. In frail patients, this has proved to be a mixed blessing: left to their own devices, subspecialists constitutionally have a narrow focus, typically merging their own interventions with what is desirable. This is not restricted to physicians: a painful lesson, oft learned, is that multidisciplinary teams do not always make for effective interprofessional collaborative practice. One useful remedy, somewhat worked out in the care of older people and sometimes used in HIV care [18], is patient-centred language and individualized outcome measurement [19].

The HIV community also offers opportunities particularly for evaluating innovative communication strategies. Younger groups of people aging with HIV represent the first "digital generation," who are likely to benefit from information and communication technologies designed to address health needs both in wealthy and resource-limited countries [20].

Particular opportunities arise in relation to polypharmacy. With the adoption of combination antiretroviral therapy (ART), most HIV-infected individuals in care are on 5 or more medications. In a geriatric medicine context, this puts them at risk of harms such as decreased medication adherence, organ system injury, hospitalization, geriatric syndromes (falls, fractures, and cognitive decline), and mortality. What can be considered as polypharmacy in HIV/AIDS? Which medications put aging people at risk? Will broad principles of de-prescribing in polypharmacy hold or require adaptationI? ID physicians have learned little by little to deal with an increasing number of comorbidities and apparently have progressively added drugs for comorbidity treatment and prevention above ARV. We still complain underprescribing of drugs like statins in HIV, but in fact overprescription of drugs is already present in HIV care [21]. Geriatric consultation often results in de-prescribing drugs rather than adding more and geriatric medicine. Even so, emerging evidence that polypharmacy per se might be less important than frailty in understanding risk in relation to medication use [22, 23].

Research tools in HIV-geriatric medicine are much needed. Current clinical trials are unlikely to inform or enhance the treatment of older HIV-positive patients. The choice of appropriate investigative clinical endpoints is important to assess the benefit of interventions, including ART therapy. The standard HIV research endpoints of virologic suppression and CD4 improvements may not be the most important tools with which to evaluate the risk/benefit ratio, even in ART clinical trials involving older HIV-positive persons. Competing non-HIV risks for death and morbidity, and greater risk for acute and chronic ARV-related toxicity, must also be considered.

The European Medical Agency recently suggested combining physical performance and patients reported in formal clinical trials (eg, using a combined outcome of walking faster than 0.8 m/s AND reporting short physical performance battery improvements) in assessing investigational drugs for treatment of sarcopenia in frail patients [24]. This seems like a useful precedent to apply to investigational antiretroviral agents for elderly people, as might also be differences in the degree of frailty between treatment groups. Geriatric assessment has been incorporated into many clinical trials, involving cancer treatment. Even so, challenges remain in using such assessments as criteria for interventional stratification or randomization, in part because of the lack of standardization of definitions of frailty and disability, and due to lack of studies about their measurement properties in clinical trials, although recently this appears to be changing. What is needed, however, is a better understanding of their responsiveness/sensitivity to change.

Every advance in medicine brings new questions and new opportunities. It is an exciting and welcome challenge now to have to address how best to care for people living with HIV as they enter old age.

Note

Potential conflicts of interest. K. R. receives career support from the Dalhousie Medical Research Foundation as the Kathryn Allen Weldon Professor of Alzheimer Research. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Now Open: Golden Compass, a Geriatric HIV Clinic

It's part of San Francisco General Hospital's Ward 86, where 1,600 of its 2,500 patients are 50 or older.

February 23, 2017

One of the first of its kind, the Golden Compass clinic specializes in geriatric care and HIV. It opened earlier this year, and already people are expressing the need to open similar clinics across the nation, reports The San Francisco Chronicle (http://www.sfchronicle.com/health/article/New-SF-General-clinic-treats-older-HIV-patients-10904711.php).

The clinic is part of San Francisco Hospital's Ward 86, which has catered to people with HIV since the epidemic began. Today, the newspaper reports, 1,600 of the 2,500 patients at the ward are 50 or older and many are long-term survivors who have been living with HIV for more than two decades. Because aging with HIV comes with its own set of challenges and questions—for example, are some symptoms related to the virus or to aging?—a unique clinic is needed.

The clinic offers specialists in aging as well as HIV, spanning cardiology, bone health, diabetes, cognitive issues and much more. Mental health and social support are stressed, as many clients experience the health effects of social isolation.

And because it's not uncommon for older people with HIV to be on as many as 20 drugs—treating everything from HIV to high blood pressure—a pharmacist at the clinic reviews prescriptions for potential drug interactions or other problems.

The clinic opened with $100,000 from AIDS Walk, which recently committed another $75,000, the Chronicle reports, but Golden Compass hopes to secure permanent funding from the city.

HIV Patients Live Longer, Require Intricate Geriatric Care

Nancy A. Melville

DALLAS - HIV adds to the typical health concerns that affect people as they age, and with fewer people dying of AIDS, healthcare providers are facing more complicated geriatric cases.

By 2030, 73% of people with HIV will be older than 50 years, according to one report (*Lancet Infect Dis*. 2015;15:753-754). But despite advances in antiretroviral therapy, life expectancies are still lower for people with HIV than for those without, according to a population-based study (*J Acquir Immune Defic Syndr*. 2016;71:213-218).

One of the key issues of concern for people with HIV is that they will develop more comorbidities as they age than uninfected people, said Kristine Erlandson, MD, from the Divisions of Infectious Diseases and Geriatric Medicine at the University of Colorado Hospital in Aurora.

Polypharmacy, which is already common in older patients, is an even greater issue in people with HIV because of their added comorbidities. And it can lead to a host of health problems.

The Problem of Polypharmacy

"We know that more medications are associated with decreased drug adherence, an increased risk of drug side effects, increased drug-to-drug interactions, and a risk for geriatric syndromes, including falls, cognitive impairment, and frailty," Dr Erlandson said here at the Association of Nurses in AIDS Care (ANAC) 2017.

The use of five or more medications is associated with increased mortality in older adults, but the association is stronger in people with HIV, according to data from one cohort of veterans (*Drugs Aging*. 2013;30:613-628).

And a recent review of 248 older San Franciscans with HIV - presented by Meredith Greene, MD, from the UCSF School of Medicine in San Francisco at the 8th International Workshop on HIV & Aging in October - showed that patients were taking a mean of 14 medications, 11 of which were not related to HIV.

Alarmingly, 16% of the patients were taking more than 20 medications, and 63% were taking at least one potentially inappropriate medication, Dr Erlandson reported.

"This is clearly a huge problem in the geriatric population of HIV-positive patients," she pointed out.

The best strategy to address polypharmacy is to enlist the help of the pharmacist.

"Have your patients take all of their medications, including supplements, over-the-counter medications, ointments, nasal sprays, eye drops - everything - to the

pharmacist, who can help sort things out," she advised. And, she added, recommend that patients use a single pharmacy for their HIV care.

When a patient presents with a complaint, clinicians should explore whether the symptoms are an adverse drug effect, a drug-drug interaction, or an underlying medical problem, Dr Erlandson said.

One resource for the latest information on drug interactions is the Beers Criteria for Inappropriate Medication Use in the Elderly, from the American Geriatrics Society, she added.

Bone Health

Bone loss is a common problem in older patients with HIV. The risk for osteoporosis that can be up to 3.7 times higher in infected than uninfected people, she reported.

Clinicians might want to avoid antiretroviral regimens that contain tenofovir disoproxil fumarate and instead use a combination of abacavir and lamivudine or tenofovir alafenamide and emtricitabine, she said.

Patients should also be evaluated for other possible contributors to osteoporosis, such as low testosterone level, low vitamin D level, phosphate wasting, hyperparathyroidism, substance use, and smoking.

Because of the increased risk for osteoporosis in older people with HIV, the risk for fracture is also elevated. The Partners HealthCare System study, which included 8525 people infected with HIV and more than 2 million uninfected people, showed that after the age of 50, fractures are significantly more common in women ($P = .002$) and men ($P < .0001$) with HIV than in those without (*J Clin Endocrinol Metab*. 2008;93:3499-3504).

Falls are the cause of many, if not most, fractures. In a study of 359 HIV-positive patients conducted by Dr Erlandson and her colleagues, 30% had fallen at least once in the previous year, and 18% had fallen more than once (*J Acquir Immune Defic Syndr*. 2012;61:484-489).

The key risk factors for falls were difficulty completing a tandem stand, defined as standing with one foot directly in front of the other, heel to toe, for 10 seconds without stumbling (odds ratio [OR], 13.5), antidepressant use (OR, 3.7), exhaustion (OR, 3.7), diabetes (OR, 3.6), and being female (OR, 3.5).

Fall prevention measures - including discontinuing medications that contribute to dizziness and exercising to improve balance and strength - can make a difference. "Tai chi has been shown to have particular benefit in some studies," Dr Erlandson noted.

Exercise can also help manage the weight gain that is associated with antiretroviral therapy and that may contribute to comorbidities such as fatty liver and diabetes, she explained.

Adults with HIV can also experience muscle loss accompanied by generalized weight

gain, leading to sarcopenic obesity. "Treatment should focus on reducing weight through dietary change and increasing muscle mass through exercise and adequate protein to maximize function," she said.

Frailty

Clinicians are probably used to resistance from patients when it comes to exercise recommendations, but they should keep in mind that older patients with HIV face unique challenges, such as greater perceived or actual fatigue, said Dr Erlandson.

Patients can feel stigmatized by their HIV status and have difficulty adopting a long-term perspective on health and wellness. And they might be in various stages of frailty, which often is "easy to recognize but hard to define," she pointed out.

The Rockwood Index and other tools can help identify frailty, but it is important to remember that it is a "multisystem clinical syndrome that reflects biologic rather than chronologic age and a vulnerability to stressors," she said.

The recent observational HAILO study showed that 6% of HIV-positive men and women aged 40 years and older were frail (*AIDS*. 2017;31:2287-2294). The risk for recurrent falls was more than 17 times greater in frail than in nonfrail patients.

"Knowing frailty status can provide an excellent assessment of fall risk," Dr Erlandson said.

Other research has shown that early intervention can significantly help frail patients.

In general, frail patients tend to have greater responses to multidomain interventions that include elements such as exercise, nutritional counseling, and — as some studies suggest — vitamin D supplementation and hormone replacement.

The care of HIV patients needs to be better coordinated, said Veronica Njie-Carr, PhD, from the University of Maryland School of Nursing in Baltimore.

In a focus group conducted at her center, patients discussed the fact that HIV practitioners should be trained in geriatric medicine, Dr Njie-Carr reported.

"This presentation validates that at the patient level," she noted.

"The patients also expressed how they have to go to one practitioner for their renal problem and another for arthritis, etc. So there clearly is the need for better coordination of care," she added.

Dr Erlandson reports receiving funding from the National Institutes of Health National Institute on Aging and research funding or speaker fees, paid to the University of Colorado, from Gilead Sciences and Theratechnologies. Dr Njie-Carr reports no relevant financial relationships.

Association of Nurses in AIDS Care (ANAC) 2017. Presented November 3, 2017.

Clinical Infectious Diseases

REVIEW ARTICLE

From One Syndrome to Many: Incorporating Geriatric Consultation Into HIV Care

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(See the Editorial Commentary by Guaraldi and Rockwood on pages 507–9.)

Antiretroviral therapy has enabled people to live long lives with human immunodeficiency virus (HIV). As a result, most HIV-infected adults in the United States are >50 years of age. In light of this changing epidemiology, HIV providers must recognize and manage multiple comorbidities and aging-related syndromes. Geriatric principles can help meet this new challenge, as preservation of function and optimization of social and psychological health are relevant to the care of aging HIV-infected adults, even those who are not yet old. Nonetheless, the field is still in its infancy. Although other subspecialties have started to explore the role of geriatricians, little is known about their role in HIV care, and few clinics have incorporated geriatricians. This article introduces basic geriatric nomenclature and principles, examines several geriatric consultation models from other subspecialties, and describes our HIV and Aging clinical program to encourage investigation of best practices for the care of this population.

Keywords. geriatric consultation; HIV; aging; NYC.

Survival among human immunodeficiency virus (HIV)–infected adults has dramatically improved with the introduction of effective antiretroviral therapy. Modeling now suggests near-normal longevity, especially for those who did not acquire HIV via injection drug use and who have restored or maintained CD4 cell counts [1]. Recent models from the Netherlands predict that >70% of HIV-infected patients will be 50 years of age or older by 2030 [2]. That same study estimates that 28% of HIV-infected patients in 2030 will have at least 3 age-related comorbidities [2]. In addition to multiple comorbidities (multimorbidity), the aging HIV-infected population is at risk for geriatric (henceforth termed aging-related) syndromes, such as frailty, falls, delirium, and functional impairment [3].

While the Centers for Disease Control and Prevention's original designation of acquired immune deficiency syndrome (AIDS) in 1982 was based on the occurrence of "a disease, at least moderately predictive of a defect in cell-mediated immunity, occurring in a person with no known cause for diminished resistance to that disease" [4], AIDS is now defined by the occurrence of opportunistic illness or nadir CD4 count <200 cells/μL in a host with HIV infection. The term "AIDS" has become anachronistic; its etiology understood, it is no longer a syndrome per se. Instead, as most persons with HIV infection are living longer lives, they are developing not only medical comorbidities but also *multiple* syndromes related to aging.

These aging-related syndromes and multimorbidity—common to elderly patients and well understood by geriatricians—may go unrecognized by HIV providers. To date, there is no formal guidance on incorporating assessment and care for these problems among HIV-infected adults. Preventive healthcare poses similar dilemmas. Cancer screening, for example, is now part of the primary care of all HIV-infected patients, but there are no guidelines on when or whether to stop preventive screening.

How can geriatric principles assist with the healthcare of this population? Awareness of these problems has increased, and there are now regional and international scientific and clinical conferences on HIV and aging, but clinical care recommendations are still largely based on expert opinion. In this article, we review the principles of aging with HIV and then examine the literature of geriatric consultation for corroborating evidence to support geriatric input in the care of people aging with HIV. We conclude with issues to consider when incorporating geriatric consultation into the care of this population.

THE IMPORTANCE OF GERIATRIC PRINCIPLES

Antiretroviral therapy has controlled HIV infection and improved quantity of life; the primary care of adults with HIV infection has become more complicated as they live longer with other, often multiple comorbidities [5]. Management of multiple

Received 12 December 2016; editorial decision 20 February 2017; accepted 3 April 2017; published online April 6, 2017.

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Clinical Infectious Diseases® 2017;65(3):501–6

DOI: 10.1093/cid/cix311

aging-related syndromes and comorbidities may require far more of the clinician's time and attention than the HIV infection itself. People aging with HIV are at risk for a diminished quality of life [6, 7]; even though they are not chronologically geriatric, they may benefit from a geriatric approach to evaluating and maintaining functional status.

How HIV infection affects aging itself is a controversial topic. The debate centers on whether HIV speeds up aging processes through established mechanisms for aging in general or whether HIV infection is an additive or synergistic risk factor [8]. Arguments for the biologic plausibility of HIV causing accelerated aging typically draw parallels between the pathophysiology of treated HIV infection and aging in general, including the prognostic significance of low CD4:CD8 ratios, potential shared immunosenescence phenotypes, and the roles of coinfections such as cytomegalovirus. A detailed discussion of this controversial topic is beyond the scope of this article and has been reviewed elsewhere [8–10]. Other approaches, such as through epigenetic analysis, are also being used to try to answer the question of whether HIV accelerates aging [11, 12].

Because the vocabulary of geriatrics and gerontology can be confusing, Table 1 provides definitions of commonly used terms. Several principles are noteworthy:

- *Aging cannot be defined or measured solely by the presence of disease*. That is not to say that aging and disease are entirely distinct, but rather that it may be deceptive to ascribe comorbidities to aging or, in the case of HIV infection, attribute increased prevalence of comorbidities to "accelerated" or "accentuated" aging.
- *The impact of multimorbidity is not the same as that of adding the impacts of multiple individual comorbidities*. Clinical practice guidelines are designed for individual diseases and are often inappropriate/unfeasible for individuals with multimorbidity [13]; optimizing therapies in a patient with multimorbidity not only requires examination of the clinical evidence but must also take patient preferences, prognosis, and clinical feasibility into account [14].
- *Aging-related (geriatric) syndromes are distinct from classic medical syndromes* [15, 16]. They are common and often seen in combination. Examples include frailty or functional decline, which are distinct from specific motor or sensorineural losses. These syndromes, rather than comorbidity, are often the primary focus of geriatric evaluation and interventions.
- *Aging-related syndromes can be seen among HIV-infected adults before they are chronologically elderly* [3]. We recommend using the term "aging-related" to increase the likelihood that providers and patients will appreciate their relevance. This is essential, as these kinds of syndromes often frame the management of the older patient who may simultaneously have several comorbidities.

Caring for people aging with HIV has required negotiating several clinical challenges. The first is the predominance of non-AIDS-defining comorbidities such as cardiac disease, renal impairment, and non-HIV malignancies as causes of chronic illness and mortality [17], leading to an increase in subspecialty consultation (eg, cardiology, nephrology, oncology) to co-manage the HIV-infected patient. The second challenge is the increased prevalence of multimorbidity, which requires coordination and prioritization of subspecialty care. The third is the high prevalence of aging-related syndromes and the need for geriatric care, even in those who are well below 65 years of age [18]. Clinical management requires preparing patients

Table 1. Aging-Related Vocabulary

Vocabulary	Definitions
Aging	A process that "is characterized by a progressive loss of physiological integrity, leading to impaired function and increased vulnerability to death" [32].
Multimorbidity	"The co-existence of 2 or more chronic conditions, where one is not necessarily more central than the others" [13].
Syndrome	A clinical condition that (unlike a disease) is of unknown etiology and is "mostly defined by a complex and often non-fixed combination of clinical signs and symptoms" [15]. The classic definition emphasizes its rarity, mystery, and multiplicity of presentations.
Geriatric or aging-related syndromes	"Clinical conditions in older persons that do not fit into discrete disease categories" and instead "cross organ systems and discipline-based boundaries" [16]. How geriatric syndromes differ from classic syndromes [15]: • They are common. • They are often defined by a single symptom (eg, urinary incontinence). • Single etiologies may precipitate multiple syndromes: falls and delirium might herald pneumonia. • Individual syndromes may have multiple etiologies: delirium might be caused by an infection, dehydration, and/or a new medication in the setting of an underlying dementia. • Older patients often have multiple geriatric syndromes at one time.
Frailty	One of the original geriatric syndromes, it is a state of diminished reserve and heightened vulnerability. Frailty has been conceptualized and measured both as a physical phenotype and as an accumulation of health deficits [33].
Basic and instrumental activities of daily living	Basic activities of daily living are basic functional tasks (eg. dressing, bathing, feeding, and transferring). Instrumental activities of daily living represent higher-order functions such as using the phone, shopping, managing medications, and finances [34].

in their 50s for healthy aging (as a way of trying to forestall or prevent these syndromes) as well as assessment and care of those who have aging-related syndromes [5].

Recognizing these new crossroads in the field of HIV medicine, the American Geriatrics Society, the American Academy of HIV Medicine, and ACRIA first published a set of guidelines in 2011 to address the management of the aging HIV population [19]. Since then, the major American HIV treatment guideline groups, the Department of Health and Human Services and the International Antiviral Society–USA, have added in small sections on aging, as well [20, 21]. However, the majority of the guidelines (although not all, eg, [22]), remain organ-based and do not address the methodology and value of geriatric consultation head-on.

GERIATRIC EVALUATION AND CONSULTATION IN OTHER SETTINGS

The history of comprehensive geriatric assessment (CGA) began with Marjorie Warren, who in the mid-20th century devised a way to triage chronically ill neglected inpatients in a hospital by creating the first geriatric assessment/treatment team. She systematically evaluated patients to determine who would benefit from medical intervention or rehabilitation efforts and was able to discharge one-third of >700 inpatient "incurables" to either home or to a residential facility [23]. Over the ensuing decades, CGA has been updated to include multiple domains (Table 2) encompassing biomedical, social, and economic concerns.

CGA has been studied both as a primary, hospital-based program and as an outpatient consultative service (integrated or separate) to other subspecialties of medicine such as cardiology [24], nephrology [25, 26], and oncology [27]. The evidence behind the effectiveness of CGA is mixed; it has resulted in improved outcomes or no effect. Geriatric evaluation has proven most valuable in inpatient settings. It has also helped clinicians prognosticate and identify problems that are often overlooked in standard medical visits. Table 3 includes recent systematic reviews and meta-analyses of studies in the general population examining the feasibility of geriatric assessment in both the outpatient and inpatient settings and the impact of CGA on treatment decision-making and outcomes (mortality and hospitalization).

Table 2. Components of Comprehensive Geriatric Assessment

Basic activities of daily living
Instrumental activities of daily living
Frailty
Nutritional status
Social network and financial status
Living situation and accessibility
Affective assessment
Cognitive assessment
Medical comorbidities
Medication appropriateness
Advance directives

CGA often provides important information when counseling about goals of care and determining the role of prevention. Eprognosis, a Web-based prognostic tool, has aggregated and assessed a number of prognostic calculators for the general older population specific to location (eg, community, nursing home) and time frame (http://eprognosis.ucsf.edu/bubbleview.php). While these calculators have not been validated specifically for HIV-infected persons, there is one mortality predictor that has been validated in the HIV population, the Veterans Aging Cohort Study (VACS) calculator (https://vacs-apps2.med.yale.edu/calculator) [28]. Although prognostically useful, the VACS calculator is not descriptive; it does not incorporate function, cognition, or direct measures of all components of multimorbidity.

The literature on geriatric consultation in other subspecialties can provide some inferences about the feasibility and usefulness of CGA. Examples of clinical models relevant to HIV care include outpatient consultative, outpatient integrative, inpatient consultation, or CGA by primary care teams as illustrated by the following representative examples.

Referral to Geriatric Clinic

Kalsi et al created an intervention where oncology patients aged 70 and older completed a screening questionnaire, and those found to be at high risk (or who were referred directly by their physician) underwent CGA by a geriatric consultant in an outpatient clinic prior to initiating chemotherapy [27]. This model was evaluated in a nonrandomized, prospective cohort study (N = 135), and patients in the intervention group were more likely than controls to complete cancer treatment. A prescreening model has been used for outpatient aging HIV patients; Ruiz and Cefalu used a CGA screen to identify appropriate patients for referral to a geriatric HIV program [29].

Assessment Within the Practice

Hall et al compared 2 models of geriatric assessment within Veterans Affairs outpatient nephrology clinics [25]. In the first model, an embedded geriatrician conducted CGA; in the second model a nephrologist with 16 hours of geriatric training or a nurse practitioner dually certified in gerontology and nephrology performed the assessments. In both models, geriatric assessment was able to identify high-impact problems such as cognitive impairment, functional impairment, and difficulty with instrumental activities of daily living (IADLs). The authors concluded that a geriatrician's treatment recommendations were necessary when nephrologists had limited experience, but that with limited training in geriatrics, nephrologists could learn how to use the basic CGA tools on their own. The authors also believed that CGA assisted in guiding care of chronic kidney disease and decisions about dialysis both by uncovering functional and cognitive problems and by identifying those who were aging well [25].

Table 3. Examples of Geriatric Assessments in Other Subspecialties

Reference and Methods	Specialty	Assessment Types	Findings
Caillet et al, 2014 [35]. Systematic review of 29 prospective observational or interventional studies. Age group: ≥65 y	Oncology	Studies included at least 5 domains of CGA	Aging-related syndromes and comorbidities were identified that could interfere with treatment or lead to death. Among a subgroup analysis of CGA, the authors estimated that that 21%–49% of treatment decisions might be affected by CGA, with nutritional status and function having the strongest effect.
Hamaker et al, 2014 [36]. Systematic review of observational cohort studies of older patients. 18 publications from 15 studies. Age group: median, 73 y	Hematologic malignancies	Geriatric assessment of at least 2 domains; median number assessed was 4 domains	ADL impairments were present in >25%; IADL impairments in 44% and depression in nearly 33% of studies. Physical function and nutritional status were associated with mortality.
Kallenberg et al, 2016 [37]. Systematic review of 30 longitudinal studies examining association between geriatric conditions and adverse outcomes. Age group: 52–84.2 y	ESRD	Assessments of functional impairment, cognitive impairment, and/or frailty	All 3 domains were associated with increase risk of mortality.
van Loon et al, 2016 [38]. Systematic review of 27 prospective studies assessing association of geriatric impairments with hospitalization or mortality in patients on or starting dialysis. Age group: 67–82 y	ESRD	At least one domain of geriatric assessment	Malnutrition, frailty, cognitive impairment, and functional impairment were associated with increased mortality. One study each links malnutrition, depression, and poor performance status to hospitalization.
Smith et al, 2016 [39]. Cochrane meta-analysis of 18 RCTs of interventions. Age group: adult	General outpatients with multimorbidity	Case coordination or multidisciplinary teamwork; or management/education interventions	Heterogeneous interventions and targets. Some evidence for improvement in mental health and functional outcomes, as well as patient and provider behaviors.
Ellis et al, 2011 [40]. Cochrane meta-analysis of 22 RCTs of hospitalized adults. Age group: ≥65 y	General inpatients	CGA by geriatric consultation teams or in geriatric units	Inpatient CGA reduces readmission, institutionalization, and mortality.

Abbreviations: ADLs, activities of daily living; CGA, comprehensive geriatric assessment; ESRD, end-stage renal disease; IADLs, instrumental activities of daily living; RCT, randomized controlled trial.

Assessment in the Home

Parlevliet and coworkers described a model where a nurse performed CGA on 50 patients on dialysis who were aged 65 years or older [26]. After completing a medical record review–based screening and sending questionnaires to be filled out by the patient and primary caregiver, the nurse then visited the patient's home and completed the CGA. Approximately 33% were found to be malnourished and 25% were depressed and/or in pain. Almost 60% had at least one IADL impairment. This model, while time-consuming, has the advantage of not requiring a geriatrician, but may not be feasible for people who do not live close to the office and do not have caregivers who can assist with the completion of forms.

Geriatric Evaluation and Consultation in Other Settings

HIV providers with limited time and geriatric knowledge focus primarily on comorbidity, antiretroviral management, and preventive care during routine visits. Whereas review described in Table 3 suggest there is value to geriatric consultation, and the above studies demonstrate feasibility of different consultation models, we do not yet know how to extrapolate these results for people aging with HIV. These populations all have serious, chronic illness in common, and it is not unreasonable to expect that CGA in people aging with HIV will uncover aging-related syndromes, prognostic information, and overlooked comorbidities, and in so doing, improve the quality of care. There are a few HIV and Aging clinical programs with published data [3, 29], but no trials that examine CGA's effectiveness in this population. With so few current geriatric models, experience with multiple programs is needed to determine the optimal approach.

CHALLENGES TO THE GERIATRIC APPROACH

Just as there is a shortage of well-trained HIV providers [30], the supply of geriatricians is insufficient [14]. As of 2012, there were 7428 board-certified geriatricians in the United States [14]. The first hurdle to creating a program is finding a geriatrician who has time, interest, and salary support to work in an HIV practice. Moreover, because many HIV-infected adults already see a multitude of specialists, the addition of yet another provider might be overwhelming to the patient or even appear to undermine the primary care provider. The mere presence of a geriatrician is no guarantee that people aging with HIV will receive adequate care. Lee et al documented that even a geriatric primary care clinic focused on memory disorders found that constraints on time and resources limited their ability to manage aging-related syndromes and multimorbidity [31]. This may imply that CGA is not enough: Training,

Table 4. Aging With HIV Program at the Center for Special Studies, New York City

The HIV and Aging Program at New York–Presbyterian Hospital/Weill Cornell Medical Center was founded in 2014 to meet the needs of patients aged ≥50 years. The program is supported in part by foundation funding and has 2 goals. The first goal is to provide integrated geriatric care within the existing Center for Special Studies human immunodeficiency virus (HIV) clinic sites. Two geriatricians offer weekly geriatric consultation alternating at our 2 clinical sites. They document in the outpatient electronic health record and attend outpatient interdisciplinary rounds at the end of the day where all patients seen that day are discussed. They communicate actively with the physicians, social workers, psychiatrists, and nutritionists to identify problems and problem-solve interventions. Inpatient consultation is also provided to clinic patients admitted to the hospital.
The second goal is to provide patient-driven education and program opportunities both within and outside of the clinic, as determined by a focus group–based needs assessment. The program offers Gold Stars, an internal social worker–driven support group that focuses on providing the space for socialization and general support while educating group participants on a variety of topics relevant to aging with HIV. In addition, the program has sponsored an arts program and links with other community-based groups to organize opportunities for patients to attend group dances and long-term survivor support groups.

collaborative structure, and access to resources are also needed to optimize care for aging adults.

INCORPORATING GERIATRICS INTO HIV CARE

When incorporating geriatrics into HIV medicine, defining the role of the geriatrician and ensuring buy-in from the primary care providers will maximize benefit and avoid additional risks to the patient from lack of coordination of care. Bringing the geriatrician to the HIV clinic is feasible. We have embedded geriatricians in a long-standing HIV clinic that already includes social work, nursing, psychiatry, gynecology, and substance abuse counseling. The program is described in Table 4. Ours is specific to New York City, but the approach to needs assessment, community engagement, and training could be applied to other programs. These are some of the factors that HIV centers should take into account:

- *Needs assessment of patients*: How do patients feel about aging? What regional, national, or cultural needs should be explored and taken into account?
- *Needs assessment of care providers*: What do staff want to learn about aging and geriatrics? How do they want to work with the geriatricians? Will they require extra in-services or backup from gerontological nurse practitioners or social workers?
- *Choosing patients for consultation*: Will there be a minimum age for consultation? Who will take priority? How will primary providers be reminded to refer? Will patients from outside your clinical program be recruited to see the geriatrician?
- *Clarifying the role of the geriatrician*: Will the geriatricians see inpatients in addition to outpatients? Should the geriatrician provide palliative care in addition to CGA?
- *Space concerns*: Where will the geriatrician see patients? How often?
- *Determination of workflow*. How will the geriatrician communicate findings and recommendations? How will the clinic staff and physicians give feedback to the geriatricians? How will the geriatrician interface with the subspecialists?
- *Salary support*: How will the physician bill? Is there foundation or institutional support for salaries?
- "*Advertising*" *the program*: Once the program begins, how will patients and providers learn about it? How will the aging program and services be publicized?
- *Collaborating with community agencies*: How will the staff reach out to other community-based organizations? How will they choose the most effective partners?
- *Creating nonclinical programs for patients aging with HIV*: Will there be over-50 support groups and/or buddy programs? Are patients asking for specific programs such as arts- or exercise-based series? How will they be funded?

CONCLUSIONS

With continued improvements in antiretroviral therapy, the HIV-infected population is growing older and aging. Although recognizing and optimizing aging-related syndromes and comorbidities are the keys to ensuring patients' quality of life, HIV care providers face time constraints and lack training in geriatric assessment. Other subspecialties have successfully adopted comprehensive geriatric assessment, and HIV care can and should do the same. We have developed one such program that may improve the functional care of our aging HIV patients, and we encourage others to create geriatrics programs that take their patients' and clinical sites' needs into account. With time, we can determine the best practices to serve our patients.

Notes

Acknowledgments. We thank the patients and leadership at the Center for Special Studies for embracing this HIV and Aging program.

Financial support. E. L. S., H. K. S., and R. F. were supported by the Fan Fox and Leslie R. Samuels Foundation.

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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BMC Geriatrics

RESEARCH ARTICLE Open Access

The increasing burden and complexity of multi-morbidity and polypharmacy in geriatric HIV patients: a cross sectional study of people aged 65 – 74 years and more than 75 years

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Abstract

Background: Geriatric Patients Living with HIV/AIDS (GEPPO) is a new prospective observational multicentre cohort consisting of all the HIV-positive geriatric patients being treated at 10 clinics in Italy, and HIV-negative controls attending a single geriatric clinic.
The aim of this analysis of the GEPPO cohort was to compare prevalence and risk factors of individual non-communicable diseases (NCD), multi-morbidity (MM) and polypharmacy (PP) amongst HIV positive and HIV negative controls at enrolment into the GEPPO cohort.

Methods: This cross-sectional study was conducted between June 2015 and May 2016. The duration of HIV infection was subdivided into three intervals: < 10, 10–20 and > 20 years. The NCD diagnoses were based on guidelines defined criteria, including cardiovascular disease, hypertension, type 2 diabetes, chronic kidney disease, dyslipidaemia, chronic obstructive pulmonary disease. MM was classified as the presence of two or more co-morbidities. The medications prescribed for the treatment of comorbidities were collected in both HIV positive and HIV negative group from patient files and were categorized using the Anatomical Therapeutic Chemical (ATC) classification. PP was defined as the presence of five or more drug components other than anti-retroviral agents.

Results: The study involved a total of 1573 patient: 1258 HIV positive and 315 HIV negative). The prevalence of individual comorbidities was similar in the two groups with the exception of dyslipidaemia, which was more frequent in the HIV-positive patients ($p < 0.01$). When the HIV-positive group was stratified based on the duration of HIV infection, most of the co-morbidities were significantly more frequent than in control patients, except for hypertension and cardiovascular disease, while COPD was more prevalent in the control group. MM and PP were both more prevalent in the HIV-positive group, respectively 64% and 37%.

Conclusions: MM and PP burden in geriatric HIV positive patients are related to longer duration of HIV-infection rather than older age per se.

Keywords: Geriatric HIV-infected population, Multi-morbidity, Polypharmacy

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Background

Aging populations are about to become the next global challenge for global public health. Advances in medicine and socio-economic development have substantially reduced morbidity and mortality due to infectious conditions and, to some extent, non-communicable diseases (NCD) [1]. Moreover, the longer survival of people with chronic conditions explains the increasing proportion of people living with NCDs. The co-existence of two or more NCDs is usually defined as multi-morbidity (MM) [2, 3]. Empirical studies based on surveys and general practice records show that MM is highly prevalent among older adults [4], and is associated with more medication prescriptions (polypharmacy, PP), the greater use of healthcare services, greater disability and mortality, and a poorer health-related quality of life [5–7]. The demographic shift has led gerontologists to recognise the different conditions that people experience during the years known as geriatric age, above 65 years. Furthermore, it has brought with it the widely used subgrouping into the youngest-old (65–74 years), the old (75–84 years), and the oldest-old (≥ 85 years) [8].

In the relatively new context of global aging, Human Immunodeficiency Virus (HIV) infection is less an exception than a paradigm. The increasing age of people living with HIV (PLWH) is the net result of increased survival due to effective antiretroviral therapy (ART) and older age at the time the infection is acquired [9]. A few studies have assessed the clinical presentation of aging HIV patients, particularly the proportion of age-related NCD affecting those aged > 50 years [10–14].

Two European cohorts (POPPY and AgeHIV) identified well-matched HIV-negative subjects. This allowed to study the impact of HIV specific risk factors such as ART exposure and toxicity, immune dysfunction or dysregulation, and chronic immune activation and inflammation [14–19]. Unfortunately, median age of these cohorts are below 50 years and none of these studies have a significant proportion of subjects of appropriately defined geriatric age.

The clinical characteristics of more than 400 patients aged > 75 years in a large French database were described at the 2016 Conference on Retroviruses and Opportunistic Infection (CROI, Boston, 22–25 February 2016). However, they acquired HIV infection at a late age (the median age at the time of starting ART being 64.5 years, range 60–70) [20]. These data have not been published so far. Therefore, the clinical presentation and aging trajectory of geriatric patients aging with HIV infection is still unknown.

Geriatric Patients Living with HIV/AIDS (GEPPO) is a new prospective observational multicentre cohort including consecutive HIV-positive geriatric patients in care at 10 HIV clinics in Northern Central and Southern Italy, and HIV-negative controls attending a single geriatric clinic.

The overall aims of the GEPPO study are to determine the health status of HIV-positive patients aged ≥65 years and its changes over time. A further aim is to investigate the extent to which the geriatric care model applies to HIV positive patients. Finally, it is intended to identify the contemporary morbidity, mortality and disability factors affecting healthy life expectancy of geriatric HIV positive patients.

In this analysis we compared prevalence and risk factors of individual non-communicable diseases, multimorbidity and polypharmacy amongst HIV positive and HIV negative controls at enrolment into the GEPPO cohort. Cross-sectional comparison was stratified by age groups, namely: youngest old (65–75) and old (≥75 years).

Methods

This is a cross-sectional analysis of HIV positive and HIV negative geriatric patients at the time of GEPPO cohort entry between June 2015 and May 2016. The patients were recruited at the time of routine follow up visit at ten HIV clinics in Northern, Central and Southern Italy with a geographical spread of 1000 Km, and were stratified into two groups: the "youngest old" (65–74 years) and the "old" (≥ 75 years). The inclusion criteria were age of ≥65 years, treatment with ART for at least six months and signed informed consent.

The HIV-negative subjects were selected from those attending a single geriatric clinic located in the same geographical area as the coordinating site (Modena). This centre offers, general practitioners support in screening NCDs in geriatric patients. The only inclusion criterion was age ≥ 65 years. Given the easy access and free of charge of any diagnostic procedure in geriatric patients, this cohort is representative of the general Italian population.

Ethics

Institutional review Board (IRB) approval was obtained from the Research Ethics Committee of each centre participating in the GEPPO cohort study. Both HIV positive and HIV negative participants gave their written informed consent, at the time of their initial visit.

Covariates

The demographic covariates and clinical outcomes of the HIV positive and HIV negative subjects were characterised and compared. They included: age, gender, BMI, smoking status. Ex- and never-smokers were grouped together and compared to current smokers. The variables considered in HIV positive patients included: current and nadir CD4 cell counts, CD4/CD8 ratio, plasma HIV RNA viral load (VL). The duration of HIV

infection was calculated as the time between diagnosis and the last visit, and was stratified into < 10, 10–20 and > 20 years. The duration of ART was calculated as the time between the start of ART and the last visit.

Outcomes

The NCDs diagnoses were based on guidelines defined criteria [21]. The cardiovascular disease (CVD) category consisted of diagnoses of myocardial infarction, coronary artery disease, peripheral vascular disease, stroke and angina pectoris, as well as coronary artery bypass grafting and angioplasty, based on records in patient files. Hypertension (HTN) was defined as two consecutive measurements of blood pressure > 140/90 mmHg or use of antihypertensive drugs. Type 2 diabetes mellitus (T2DM) was defined as fasting serum glucose levels ≥126 mg/dL or use of antidiabetic drugs. Chronic kidney disease (CKD) was confirmed at an estimated glomerular filtration rate (eGFR) of < 60 mL/min calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi) equation mL/min/1.73 m2. Dyslipidaemia (DLM) was defined in patients with fasting total cholesterol levels > 200 mg/dL or triglyceride levels of > 150 mg/dL or the current use of statins. Diagnosis of HTN, CKD and DLM were confirmed in two consecutive measurements. Chronic obstructive pulmonary disease (COPD) was defined based on pulmonary function tests (spirometry, diffusion capacity of carbon monoxide [DLCO]) demonstrating FEV_1/forced vital capacity (FVC) ratios < 70%. MM was defined as the presence of two or more NCDs [2, 3].

The medications prescribed for the treatment of NCDs were collected from patient files in both HIV positive and HIV negative groups and were categorized using the Anatomical Therapeutic Chemical (ATC) classification in which the drugs are divided into different groups based on therapeutic indication [22]. The analysis considered the prevalence of the six most frequently prescribed classes other than ART with particular regards of cardiovascular active agents including statins, beta-blocker, ACE-inhibitors, anti-hypertensives and acetylsalicylic acid (ASA) and psychoactive agents including benzodiazepines (BDZ).

Polypharmacy was defined as the presence of five or more drug components other than ART. The decision not to include ART was due to the need to compare HIV-positive and HIV-negative subjects.

Statistical analysis

In the participating Centres the study size of the HIV-positive patients was represented by the whole of HIV infected patients meeting inclusion criteria, who presented at routine medical visits in the enrolment period (year 2015).

Per protocol the two groups were matched for age (±4 years) within male and female groups through a 4:1 ratio, using random selection. A reduced number of HIV negative people were chosen with a view to the large sample size of HIV patients.

Missing data on outcomes were indicated in the tables as different denominators for parentage values.

The between-group comparisons were made using the χ^2 test for categorical variables, and the t test or Mann-Whitney U-test for the normally and non-normally distributed continuous variables respectively.

The probability of MM and PP at each age was compared in the HIV-negative controls and the HIV-positive patients stratified as of the duration of HIV infection (< 10, 10–20 and > 20 years). These times were chosen for two main reasons. Firstly they paralleled the tertile distribution of this variable. Secondly, they identified the subsets of subjects aging since the pre-ART, and the early and the late-ART periods.

Multivariable logistic regression models were built to predict MM and PP including the following as covariates: age categories, gender, BMI, current smoke and duration of HIV infection, using HIV negative as reference.

A second model was restricted to HIV patients including HIV related variables such as: current CD4, CD4 Nadir, CD4/CD8 ratio, HIV-1 VL undetectability (< 40 copies/mL), and residual of ART duration after adjustment for HIV infection duration.

Residual ART duration was calculated through univariate linear regression between ART exposure and duration of HIV infection. This was performed to avoid co-linearity between these two variables.

Statistical analyses were performed using the “R” Software, version 3·2.

Results

The study involved a total of 1573 patient (1258 HIV positive and 315 HIV negative). The HIV-positive patients aged 65–74 and ≥ 75 respectively represented 3.8% and 0.5% of the HIV-positive populations at the GEPPO recruiting sites.

With regards to demographic and anthropometric variables, mean age was 72 (SD = 4.27) years for men and 71 (SD = 3.94) years for women. HIV positive individuals were thinner and more frequent smokers. In the group of individuals above the age of 75 HIV negative had the same prevalence of smoke habits as HIV-positive ones (10.84% vs 15.23%, $p = 0.39$) (Table 1).

With regards to HIV variables mean HIV duration of 17 years. However, 33% of them had HIV exposure for more than 20 years, representing people aging with HIV from the pre-ART era. The age at HIV diagnosis was significantly higher (60.3 ± 7.6 vs 52.1 ± 8.2) in “old” individuals compared to “youngest old” HIV people ($p < 0.01$).

Table 1 Demographic, anthropometric and HIV variables in the GEPPO cohort

	Total $n = 1573$	HIV-negative vs HIV-positive			HIV-negative			HIV-positive		
		HIV- ($n = 315$, 20·03%)	HIV+ ($n = 1258$, 79·97%)	p	65–74 years ($n = 224$, 71·11%)	≥ 75 years ($n = 91$, 28·89%)	p	65–74 years ($n = 965$, 76·71%)	≥ 75 years ($n = 293$, 23·29%)	p
Variable	Mean (SD) [sample size]	Mean (SD/%) [sample size]			Mean (SD/%) [sample size]			Mean (SD/%) [sample size]		
Gender (F)	271 (17.23%) [1573]	66 (20.95%) [315]	205 (16.3%) [1258]	0.06 *	42 (18.75%) [224]	24 (26.37%) [91]	0·18 *	155 (16.06%) [965]	50 (15.06%) [293]	0.75 *
Female Age	71.23 (3.94) [271]	71.55 (3.42) [66]	71.15 (4.05) [205]	0.12 ***	69.83 (2.48) [182]	77.46 (2.08) [67]	< 0.01***	69.46 (2.52) [810]	77.5 (2.0) [243]	< 0.01***
Male Age	71.71 (4.27) [1302]	72.61 (4.37) [249]	71.42 (4.21) [1053]	0.06 ***	70.05 (2.75) [42]	75.61 (0.49) [25]	< 0.01***	69.35 (2.48) [155]	77.17 (1.) [50]	< 0.01***
BMI	26.55 (8.59) [1224]	28.65 (4.18) [301]	25.87 (9.5) [923]	< 0.01 ***	28.71 (4.04) [8]	28.52 (4.54) [6]	0.65 ***	26.15 (10.66) [264]	24.98 (3.95) [71]	0.04 ***
Current smoker	313 (23.29%) [1344]	42 (14.24%) [295]	271 (25.83%) [1049]	< 0.01*	33 (15.57%) [212]	9 (10.84%) [83]	0.39 *	234 (29.03%) [806]	37 (15.23%) [243]	< 0.01*
HIV duration (years)	NA	NA	17.17 (7.65) [1240]	NA	NA	NA	NA	17.24 (7.76) [949]	16.92 (7.3) [291]	0·64 **
< 10 years	NA	NA	263 (21.23%) [1240]	NA	NA	NA	NA	200 (21·07%) [949]	63 (21.72%) [291]	0·9*
10–20 years	NA	NA	561 (45.28%) [1240]	NA	NA	NA	NA	433 (45.63%) [949]	128 (44.14%) [291]	
> 20 years	NA	NA	415 (33.49%) [1240]	NA	NA	NA	NA	316 (33.3%) [949]	99 (34.14%) [291]	
CD4 nadir	NA	NA	197.5 (84–310) [1240]	NA	NA	NA	NA	200 (89.75–308) [949]	191 (74.75–320) [291]	0·61 **
Current CD4	NA	NA	644.58 (1240) [1258]	NA	NA	NA	NA	651.23 (290.95) [949]	622.55 (282) [291]	0·18 **
CD4/CD8	NA	NA	0.97 (1.45) [1240]	NA	NA	NA	NA	0.92 (0.8) [949]	1.13 (2.63) [291]	0·28 ***
Viral load ≤40	NA	NA	1044 (94.31%) [1107]	NA	NA	NA	NA	812 (94.97%) [855]	232 (92.06%) [252]	0.11 *
Viral load undetectable	NA	NA	925 (86.53%) [1068]	NA	NA	NA	NA	712 (86.72%) [821]	213 (85.89%) [248]	0.82 *
HBV co-infection	NAv	NAv	103 (9.83%) [1048]	NAv	NAv	NAv	NAv	84 (10.51%) [799]	19 (7.63%) [249]	0·23*
HCV co-infection	NAv	NAv	141 (12.57%) [1121]	NAv	NAv	NAv	NAv	113 (13·11%) [862]	28 (10·77%) [259]	0·12 *
Age at HIV diagnosis	NA	NA	54·03 (8.83) [1239]	NA	NA	NA	NA	52·11 (8.28) [949]	60·3 (7.6) [290]	< 0·01***
Triple/M ART	NA	NA	390 (31.91%) [1222]	NA	NA	NA	NA	312 (31.01%) [1006]	78 (36.11%) [216]	0·17 *
Mono/dual ART	NA	NA	832 (68.09%) [1221]	NA	NA	NA	NA	694 (68.99%) [1006]	138 (63.89%) [215]	

Abbreviations: *ART*: AntiRetroviral Therapy; *BMI*: Body Mass Index; *HIV*: Human Immunodeficiency Virus; *NA*: not applicable. *NAv*: not available;
p value legends: * X2 test; ** Wilcoxon; *** t test

HIV positive patients had well recovered immune status, as assessed with a mean CD4/CD8 equal to 0.97 and reached HIV-RNA viral load below 40 copies/mL in 94%. Hepatitis C and B co-infection were 13% and 10% respectively (Table 1).

NCDs, MM and PP prevalence increased with age categories with the exception of T2DM and dyslipidaemia in HIV negative patients only (Table 2).

The overall prevalence of MM and PP respectively amounted to 64% and 37% in HIV-positive patients, and 59% and 24% in controls.

In "youngest old" group CKD, DLM and PP only were more prevalent in HIV positive patients; the same was true in the "old" group for T2DM, DLM and CKD (Table 2).

When the HIV-positive group was stratified by duration of HIV infection, individual comorbidities were significantly more frequent in the HIV-positive subgroups with HIV exposure> 10 years when compared to HIV negative, except for HTN and CVD. The prevalence of COPD was higher in the controls (fig. 1).

Probability of MM was higher in HIV positive patients aging with HIV for more than 10 years when compared to HIV negative controls (fig. 2a). Independent predictors for MM were age > 75 years, higher BMI, male gender and HIV duration above 20 years, all $p < 0.01$

Table 2 NCDs prevalence comparing "youngest old" and "old" individuals

	65–74 Years Old			≥ 75 Years Old		
	HIV- (*n* = 224, 18.84%)	HIV+ (*n* = 965, 81.16%)	*p*	HIV- (*n* = 91, 23.7%)	HIV+ (*n* = 293, 76.3%)	*p*
Variable	Frequency [sample size]			Frequency [sample size]		
HTN	149 (66.52%) [224]	396 (60.83%) [652]	0.15	61 (67.03%) [91]	155 (71.76%) [216]	0.49
T2DM	50 (22.32%) [224]	176 (27.54%) [629]	0.15	14 (15.38%) [91]	65 (31.25%) [208]	< 0.01
CVD	41 (18.3%) [224]	106 (16.88%) [628]	0.70	28 (30.77%) [91]	58 (29.15%) [199]	0.88
CKD	5 (5%) [100]	115 (17.06%) [674]	< 0.01	4 (10%) [40]	56 (25.93%) [216]	0.04
COPD	20 (9.13%) [219]	41 (6.61%) [620]	0.28	17 (18.89%) [90]	19 (9.79%) [194]	0.05
DLM	59 (57.84%) [102]	462 (70%) [630]	0.02	20 (50%) [40]	156 (74.64%) [209]	< 0.01
MM	57 (57.58%) [99]	371 (61.32%) [605]	0.55	25 (62.5%) [40]	139 (73.94%) [188]	0.20
PP	44 (19.64%) [224]	169 (35.28%) [479]	< 0.01	32 (35.16%) [91]	73 (42.94%) [170]	0.27

Abbreviations: *HTN*: Hypertension; *T2DM*: type 2 diabetes mellitus; *CVD*: Cardiovascular Disease; *CKD*: Chronic Kidney Disease; *COPD*: Chronic Obstructive Pulmonary Disease; *DLM*: Dyslipidaemia; *MM*: Multimorbidity; PP - Polypharmacy

(fig. 2b). A second model restricted to HIV patients only (data not presented in fig. 2), while confirming the same predictors of the previous model, failed to identify any association between traditional HIV variables and MM. In particular: current CD4/CD8 OR = 1.53 (95% CI:0.97–2.43, $p = 0.07$), CD4 nadir OR = 1 (95% CI: 1–1, $p = 0.83$), HIV RNA undetectability OR = 1.37 (95% CI:0.65–3.04, $p = 0.42$) and residual ARV exposure duration OR = 0.97 (95% CI:0.9–1.05, $p = 0.45$).

We examined in the GEPPO cohort the six most frequently prescribed drug classes for the treatment of NCDs. There was no difference in the prescription of and antidepressants or acetylsalicylic acid (ASA), ace-inhibitors (ACE) and beta-blockers, commonly used in primary or secondary cardiovascular disease prevention. A higher prescription of benzodiazepines (BDZ), used as sleep inducers, was present in HIV negative people ($p < 0.01$), while a higher prescription of statins for dyslipidaemia in HIV positive patients was observed ($p < 0.01$) (fig. 3a). PP was higher in HIV positives, irrespective of duration of HIV-infection (Fig. 3b).

At any age PP was more common in HIV patients (fig. 4a). Drivers for higher PP risk were HIV duration

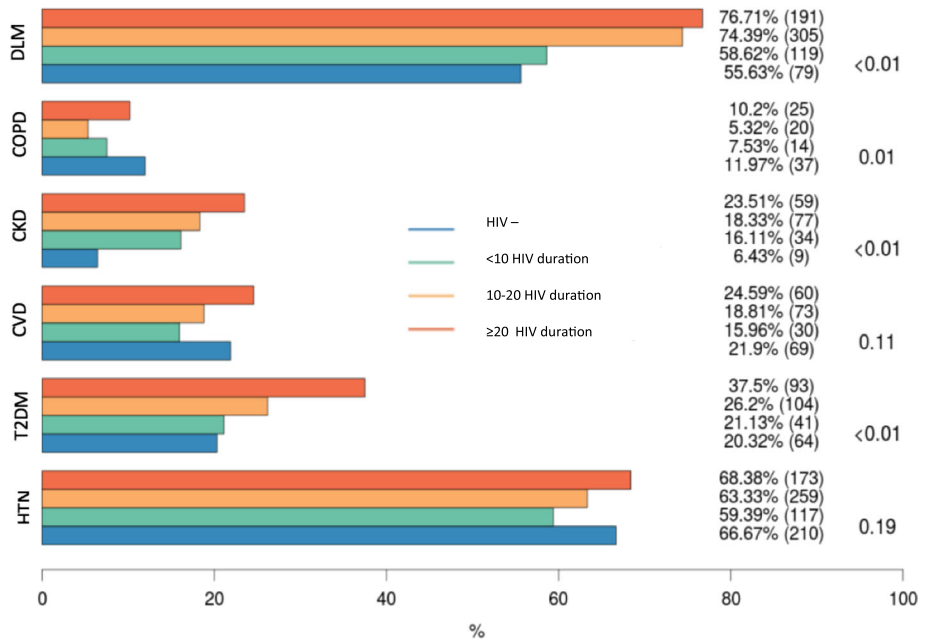

Fig. 1 Prevalence of NCDs in the cohort as a whole, and in three HIV duration groups (< 10, 10–20 and > 20 years). NCDs prevalence (%) and absolute numbers (n) are indicated for HIV negative and HIV positive with different HIV duration groups. Indicated *p*-value refers to HIV-positive versus HIV-negative comparison. Abbreviations DLM: Dyslipidaemia; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease; CVD: Cardiovascular Disease; T2DM: Type 2 Diabetes mellitus.HTN: Hypertension

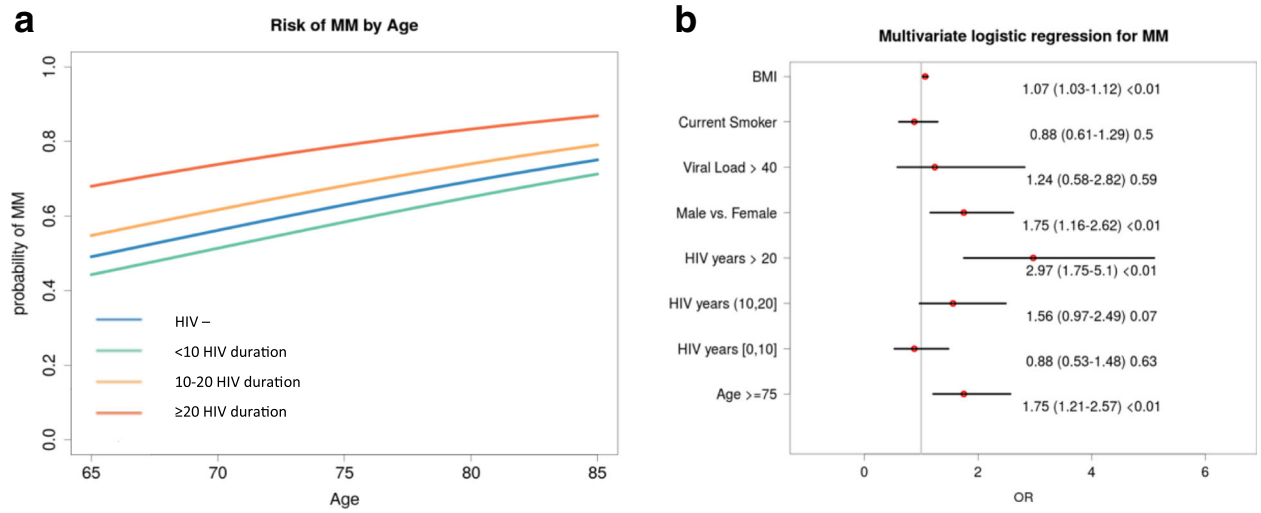

Fig. 2 a Probability of MM per year above the age of 65. The HIV positive patients are stratified by duration of HIV infection (< 10, 10–20 and > 20 years). **b** Multivariable logistic regression models to detect the independent predictors of MM. Abbreviations – MM: Multimorbidity

with progressive OR increase per increment of HIV duration category and age above 75 years (fig. 4b).

A second model restricted to HIV patients only (data non-presented in fig. 4), while confirming the same predictors of the previous model, failed to identify any association between traditional HIV variables and PP. In particular: current CD4/CD8 OR = 0.83 (95% CI:0.44–1.52, $p = 0.54$), CD4 nadir OR = 1 (95% CI:1–1, $p = 0.73$), HIV RNA undetectability OR = 1.75 (95% CI: 0.91–3.48, $p = 0.1$) and residual ARV exposure duration OR = 1.03 (95% CI:0.93–1.13, $p = 0.61$). Significant predictors identified in the original model were confirmed.

Discussion

Our findings indicate that MM and PP in HIV-positive individuals are both related to longer duration of HIV-infection rather than older age per se.

People aging with HIV for more than 20 years are almost three times as likely to have MM than those infected for a shorter period.

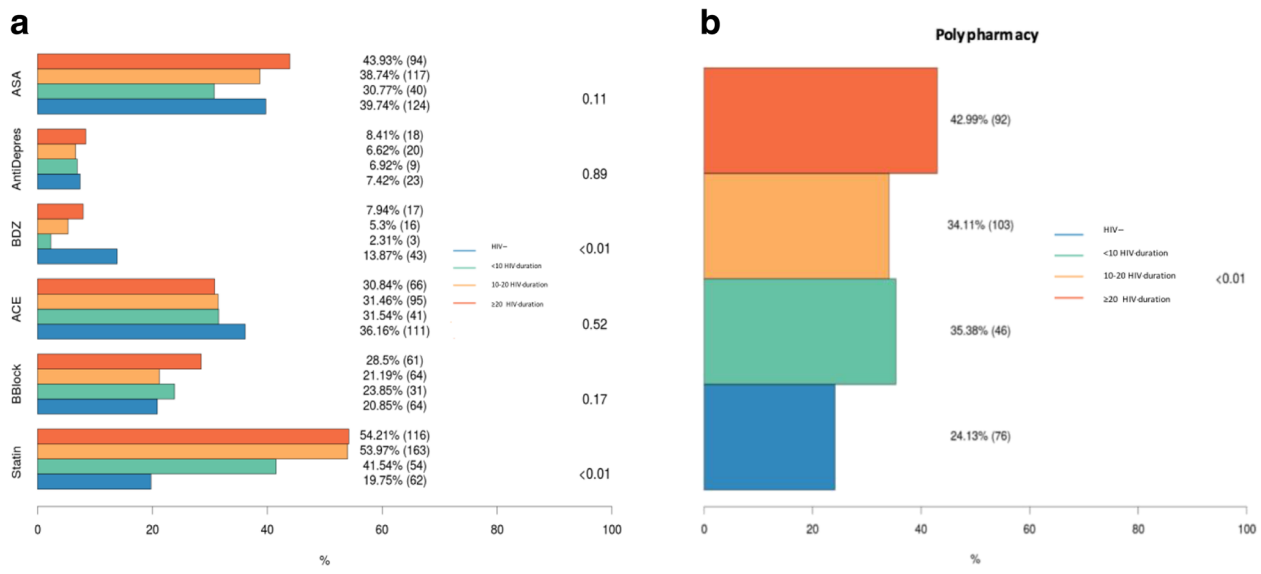

Fig. 3 a Prevalence of the six drug classes most frequently prescribed for the treatment of NCdD and **b** prevalence of PP in HIV negative and HIV positive stratified by duration of HIV infection (< 10, 10–20 and > 20 years). Drug classes prevalence (%) and absolute numbers (n) are indicated for HIV negative and HIV positive with different HIV duration groups. Indicated p-value refers to HIV-positive versus HIV-negative comparison. Abbreviations – ASA: acetylsalicylic acid; AntiDepres: antidepressants; BZD: benzodiazepines; ACE; Angiotensin Converting Enzyme inhibitors; BBlock: beta-adrenergic blocking agents; Statine: statins

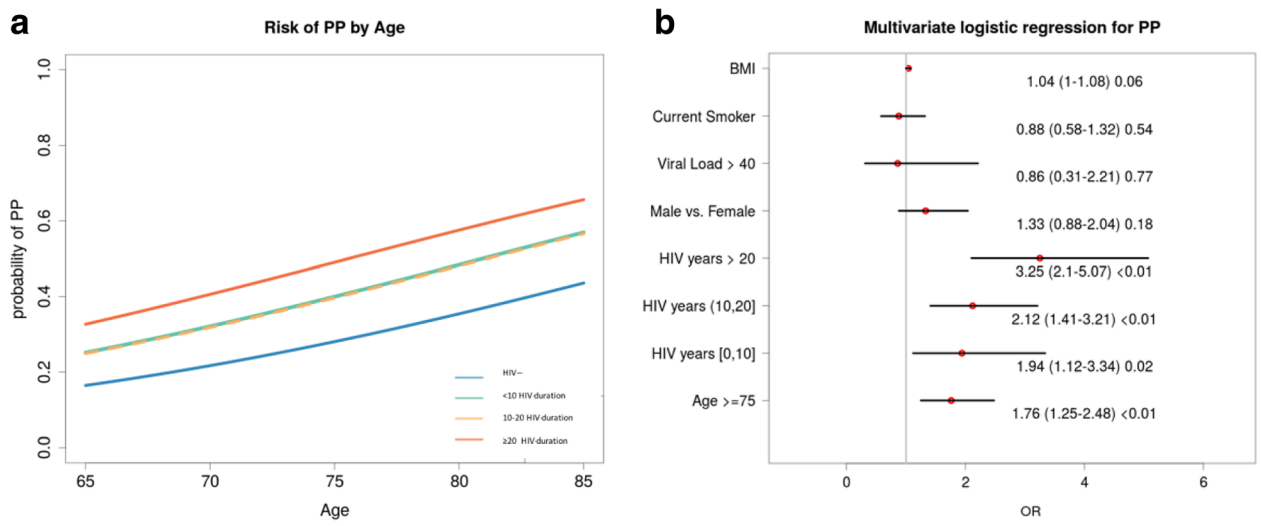

Fig. 4 a Probability of PP per year above the age of 65. The HIV positive patients are stratified by duration of HIV infection (< 10, 10–20 and > 20 years). **b** Multivariable logistic regression models to detect the independent predictors of PP.Abbreviations – PP: polypharmacy

It can be noticed that HIV positive patients belonging to the GEPPO cohort who have been living with HIV for more than 20 years were all exposed to the first generation of ART. These are "silver champions", since they represent the best survivors of their generation and warrant as much attention as geriatric medicine has paid to centenarians, possibly identifying protective factors for NCDs.

These individuals have been exposed for years to detectable VL in the pre-ART era and have received highly toxic ART, both of them representing a permanent risk of NCDs.

However, it must be acknowledged that this phenomenon may change in future years. The START trial, a large randomized clinical trial conducted in 35 countries enrolling over 4500 HIV+ ART-naïve subjects randomized to immediate (CD4 ≥ 500/μL) or deferred ART initiation (CD4 < 350/μL) demonstrated that immediate ART reduced incidence of NCDs, pointing to the role of long-term immune activation and inflammation. In the contemporary setting of immediate access to new-generation ART, it can be hypothesised that the prevalence of NCDs and MM will be reduced in the years to come [23].

The prevalence of comorbidities was different in the HIV-positive patients and controls. The higher prevalence of DLM, CKD and T2DM has been widely described [12], and can at least partially be attributed to the metabolic toxicities of ART [24–26]. COPD was more prevalent in the HIV-negative individuals. This is somewhat surprising considering the higher proportion of smokers among HIV positive patients (26% vs 14%), and it suggests that infectious diseases physicians are less likely to use spirometry to screen HIV positive patients. The European AIDS Clinical Society (EACS) guidelines have only recently introduced COPD as a comorbid condition that should be screened for [21]. There was no difference in the prevalence of CVD or HTN as has been observed in other cohorts [27], possibly due to strategies used to reduce CV risk factors, the increasing use of lipid-friendly ART agents, and reduction of immunodeficiency state.

Most of the participants of the GEPPO cohort have MM (59%), this appears to be the norm in HIV-infected geriatric patients [9]. We still need research to investigate the multifactorial nature of MM and the impact of this condition on quality of life, functional status impairment, health service use, and mortality. This will help healthcare services to address the unmet needs of PLWH with MM.

HIV, proportionally with its duration is a risk factor for PP. HIV positive patients have been visiting physicians since a young age and PP may be the result of the "medicalisation" of early diagnosis of NCDs.

MM and PP were both more prevalent in the HIV-positive group, respectively 64% and 37%. The increased burden of PP in this HIV cohort is striking, particularly in the light our very restrictive definition of PP (the chronic use of five or more drugs, excluding ART). The greater the number of medicines patient takes, the greater the risk of adverse effects, and the greater the risk of drug–drug interactions, leading to poor health outcomes, hospitalisations and mortality [28]. This is a dilemma for prescribers, who try to keep the number of medicines to a minimum while ensuring that patients receive what evidence-based guidelines advocate as being in their best interest [29].

Apparently, ID physicians and geriatricians use different drugs to treat the same comorbidities. An important

difference regards the use of statins. Studies have underlined the need to increase statin prescription in HIV-positive patients due to increased cardiovascular risk. However, the use of statins in the elderly is a concern in the context of sarcopenia and fall risk [30]. Possibly geriatricians more than ID physicians are more concerned of this issue and this may be reflected by the fewer statin prescriptions received by the HIV negative controls in the GEPPO cohort.

Benzodiazepines were prescribed more frequently in the HIV negative than for the HIV positive patients. This may reflect the aversion of former intravenous drug users to use psychoactive drugs that may induce dependence.

With regard to gender, the prevalence and risk of MM (but not PP) was higher among males.

As expected males had increased risk of comorbidities but this was not the same for PP in the Italian national health system context were drugs for NCDs are provided for free in geriatric patients. The risks of MM and PP were different in the subjects aged more or less than 75 years. Apparently, the "younger-old" and "old" geriatric categories cover two subsets of elderly people with different risk profiles, and this must also be considered in HIV-positive patients.

Our data claim for a tailored approach to NCDs, and highlight the development of drug de-prescription strategies in the management of PP. Although de-prescribing is relatively new in HIV medicine, the use of the Beers criteria [31], IPET (Improving Prescribing in the Elderly Tool) [32] and STOPP-START criteria [33, 34] to adjust therapy and reduce potentially inappropriate drugs is well established in geriatric practice, and should be extended to the HIV setting [35].The benefit of de-prescribing in HIV positive geriatric patients has never been evaluated so far.

The GEPPO cohort includes HIV-positive patients aged ≥65 attending ten HIV clinics across Italy (who, taken together, makes a quite significant absolute number of elderly people living with HIV) and a group of age and gender-matched HIV-negative controls attending a single geriatric clinic. People of this age frequently visit geriatric clinics because of age-related comorbidities. Therefore, our cohort provides a new opportunity to compare HIV-infected patients with HIV-negative controls better representative of the general population than subjects attending centres for sexually transmitted diseases or intravenous drug user facilities used in previous studies.

This study has a number of limitations. Some of these are intrinsic to cross-sectional nature of observational studies, which cannot reveal any causative association between variables. The prevalence of comorbidities, although standardized in cohort studies may overestimate disease condition. This is the case of DLM, where use of statins is used as diagnostic criteria. We found no significant difference of HIV-related variables other than the duration of HIV infection to be associated with the risk of MM or PP. For this reason, ART exposure was not considered as a covariate, also because it requires properly designed clinically study. Cumulative smoke pack year was not addressed, because not routinely collected in all the clinics. A major limitation of this study was the lack of information on geriatric syndrome, including frailty and falls. Geriatric syndromes, better than NCDs capture the healthy aging outcome that all geriatric studies should address (ref). This information will be available in future studies of GEPPO cohort.

To the best of our knowledge, the GEPPO is the first geriatric cohort of HIV-positive patients that may contribute to identify unmet clinical and research needs in terms of comorbidities and their implications for PP. This model highlights the need for evidence-based screening and monitoring protocols to ensure high-quality care.

Conclusions

The findings of this study show MM and PP burden in geriatric HIV positive patients are related to longer duration of HIV-infection rather than older age per se.

Acknowledgements

Authors are grateful for help in data collection to: Liliana Maia, MD, Department of Infectious Diseases of Centro Hospitalar do Porto, Portugal. Morena Valentina, MD and Elena Gervasi MD, Third Division of Infectious Diseases, University of Milan, Ospedale L. Sacco, Milan, Italy. Paola Magro, MD and Eugenia Quiros Roldan, MD, Unit of Infectious and Tropical Diseases, University of Brescia. Andrea Marino, MD, Department of Clinical and Molecular Biomedicine, Division of Infectious Diseases, University of Catania, ARNAS Garibaldi, Catania, Italy.

Funding

This study was not sponsored. This study was carried out as part of the authors routine work.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

GG, MA, CA, MC, CBM, CF, PS, DSGV, CAM, OG, RA, FA, NS, DPG contributed to study design, data collection and revision. GG also did supervision and writing. MA was also the data manager and the person in charge of statistical analyses. All authors read and approved the final manuscript.

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Giovanni Guaraldi, MD, is Associate Professor of Infectious disease at the University of Modena and Reggio Emilia. Since the year 2000, he has lead the Modena HIV Metabolic Clinic (MHMC). This referral centre offers a multidisciplinary team approach to HIV patients with metabolic abnormalities, and it offers a multidimensional evaluation of ageing HIV infected patients. More than 4500 patients are followed at this Centre.
Prof. Guaraldi published over 300 peer reviewed papers mainly focused on frailty and HIV associated co-morbidities.
In 2016 he built the first HIV geriatric cohort in Italy called: Geriatric Patients Living with HIV/AIDS (GEPPO).
Two peer reviewed papers have been published.
about this new prospective observational multicentre cohort:

1. Calcagno A, Piconi S, Focà E, Nozza S, Carli F, Montrucchio C, Cattelan AM, Orofino G, Celesia BM, Morena V, De Socio GV, Guaraldi G; **GEPPO (GEriatric Patients living with HIV/AIDS: a Prospective Multidimensional cOhort)** Study Group. Role of

Normalized T-Cell Subsets in Predicting Comorbidities in a Large Cohort of Geriatric HIV-infected Patient. J Acquir Immune Defic Syndr. 2017 Jul 8. doi: https://doi.org/10.1097/QAI.0000000000001496. [Epub ahead of print]
2. Nozza S, Malagoli A, Maia L, Calcagno A, Focà E, De Socio G, Piconi S, Orofino G, Cattelan AM, Celesia BM, Gervasi E, Guaraldi G; **GEPPO Study Group. Antiretroviral therapy in geriatric HIV patients: the GEPPO cohort study.** J Antimicrob Chemother. 2017 Jun 10. doi: https://doi.org/10.1093/jac/dkx169. [Epub ahead of print] PMID:28605493

Ethics approval and consent to participate
The study received approval from Comitato Etico Provinciale di Modena. Study 39/2016. IRB approval: Prot.1710 of 10 May 2016.
Written informed consent was obtained from participants.

Consent for publication
The paper contains aggregated data only.

Competing interests
GG received research grants from ViiV Healthcare, Gilead, Merck Sharp and Dohme (MSD). Talks grants from ViiV Healthcare, Gilead, Merck Sharp and Dohme, Jansen, BMS. Consultation to ViiV Healthcare, Gilead, Merck Sharp and Dohme. CA received grants, travel grants and speaker's honoraria from Abbvie, BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. CBM received grants, travel grants and speaker's honoraria from Abbvie, BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. DSGV received travel grants from Abbvie, BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. CAM received grants and speaker's honoraria from Abbvie, BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. NS received travel grants and speaker's honoraria from Abbvie, BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. OG received travel grants and speaker's honoraria from Abbvie, BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. RA grants, travel grants and speaker's honoraria from BMS, Gilead, ViiV Healthcare, Janssen-Cilag, Novartis and MSD. FE received travel grants and speaker's honoraria from BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. DPG received grants, travel grants and speaker's honoraria from Abbvie, BMS, Gilead, ViiV Healthcare, Janssen-Cilag and MSD. MA, MC, CF, PS reported no potential conflict of interest.

Publisher's Note

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Received: 26 July 2017 Accepted: 12 April 2018
Published online: 20 April 2018

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