


# Long-acting drugs: people's expectations and physicians' preparedness. Are we readying to manage it? An Italian survey

Marta Celesia, DEC<sup>a</sup>, Vittoria Moscat, MD<sup>b,c</sup>, Alessandra Tzannis, DEC, PhD<sup>a</sup>, Michele Trezzi, MD<sup>d</sup>, Emanuele Focà, MD, PhD<sup>e</sup>, Margherita Errico<sup>f</sup>, Paola Cinque, MD, PhD<sup>g</sup>, Silvia Nozza, MD, PhD<sup>g</sup>, Antonella Cingolani, MD, PhD<sup>h</sup>, Manuela Ceccarelli, MD<sup>b,i,\*</sup> , Benedetto M. Celesia, MD, PhD<sup>j</sup>, and for the LAI Italian Survey Research Group

## Abstract

To evaluate patients' expectations regarding long-acting antiretroviral agents and preferences about where to receive them. Multicenter cross-sectional survey-based study. Through an online survey, we asked people living with human immunodeficiency virus to judge their relationship with daily antiretroviral therapy (ART) and to give their opinion about long-acting drugs. We also collected data regarding the age of the patients, their site of follow-up, time since the diagnosis, and compliance to ART. Two hundred forty-two patients aged 18 to 79 years were included in the study: 58 (24%) females, 182 (75.2%) males, and 2 (0.8%) male-to-female transgenders. 81.8% of the said population had a good relationship with ART. 33.6% of them consider daily ART an obligation and a restriction to their freedom. One hundred forty-three (59.1%) patients already knew about long-acting drugs before our interview, and 215 (88.8%) patients were interested in it. One hundred fifty-six (64.4%) interviewees said they would still be interested in hospital-available injective long-acting drugs, although 57.9% of the patients would rather receive them at home. The data emerging from our survey reveal that around 90% of the people living with HIV are interested in changing their actual treatment with a long-acting one. Moreover, for the first time to our knowledge, such a high number of patients showed an enthusiastic response to the new opportunity to be treated directly at home. The introduction of these new drugs could be revolutionary and represents an important step toward treatment simplification.

**Abbreviations:** cART = combined antiretroviral therapy, HIV = human immunodeficiency virus, LAI = long-acting injectable, PLWH = people living with HIV, STR = single tablet regimen.

**Keywords:** antiretroviral therapy, ART, cART, HIV, long-acting drugs, survey

## 1. Introduction

Combined antiretroviral therapy (cART) completely changed the prognosis of human immunodeficiency virus (HIV) infection improving the survival of people living with HIV (PLWH) as much as their quality of life.<sup>[1]</sup> Acquired immunodeficiency syndrome is no longer the inevitable outcome of HIV infection in countries with good access to treatment.<sup>[2]</sup>

cART currently requires daily oral administration that can be perceived as a burden by many patients as it results in a variable pill amount according to the prescribed regimen.<sup>[3]</sup> Given the need for life-long treatment, successful cART requires a

person's readiness to start and adhere to treatment over time.<sup>[4]</sup> Despite the availability of single tablet regimens (STRs) perfect adherence is still dependent on the patient and on their perception of the infection and therapy.<sup>[5]</sup> In our experience, up to 50% of PLWH referred at least 1 episode of nonadherence per year.

Modern cART is characterized by a higher grade of forgiveness than the regimens available in the past.<sup>[5]</sup> As a matter of fact, we have now drugs with higher genetic barrier to resistance and longer half-life. The causes of suboptimal cART adherence may be different varying from therapy or healthcare-related factors to psychosocial ones.<sup>[3]</sup>

The authors have no funding and conflicts of interest to disclose.

Data can be accessed at the corresponding author upon reasonable requests.

Supplemental Digital Content is available for this article.

<sup>a</sup> Economics and Business Management/Service Management, Università Cattolica del Sacro Cuore, Milan, Italy, <sup>b</sup> Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Catania, Catania, Italy, <sup>c</sup> Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Messina, Messina, Italy, <sup>d</sup> Unit of Infectious Diseases, Ospedale San Jacopo – Pistoia – AUSL 3, Pistoia, Italy, <sup>e</sup> Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy, <sup>f</sup> Network Persone Sieropositive Italia, Milan, Italy, <sup>g</sup> Unit of Infectious Diseases, IRCCS S. Raffaele Hospital, Milan, Italy, <sup>h</sup> Department of Laboratory and Infectious Disease Sciences, Unit of Infectious Diseases, IRCCS Policlinico Universitario Gemelli, Rome, Italy, <sup>i</sup> Department of Biomedical, Dental, Morphological and Functional Imaging Sciences, University of Messina, Messina, Italy, <sup>j</sup> Unit of Infectious Diseases, ARNAS Garibaldi, Nesima Hospital, Catania, Italy.

\* Correspondence: Manuela Ceccarelli, Department of Clinical and Experimental Medicine, Unit of Infectious Diseases, University of Catania, c/o ARNAS Garibaldi – Nesima Hospital, Hospice Building, Via Palermo 636, Catania 95122, Italy (e-mail: manuela.ceccarelli@unict.it).

Copyright © 2022 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Celesia M, Moscat V, Tzannis A, Trezzi M, Focà E, Errico M, Cinque P, Nozza S, Cingolani A, Ceccarelli M, Celesia BM. Long-acting drugs: People's expectations and physicians' preparedness. Are we readying to manage it? An Italian Survey. *Medicine* 2022;101:42(e30052).

Received: 27 July 2021 / Received in final form: 6 April 2022 / Accepted: 23 April 2022

<http://dx.doi.org/10.1097/MD.00000000000030052>

The need of raising patients' compliance to 100%, combined with the availability of drugs with longer half-lives and new methods of administration, led scientists worldwide to focus their research on the introduction of long-acting injectable (LAI) antiretroviral drugs. In fact, eliminating the need for daily administration, LAI may have a potential role in solving some challenges such as confidentiality concerns related to stigma and discrimination, HIV infection-related anxiety, medical difficulty in oral administration, pill fatigue, and risk of treatment failure and HIV transmission.

Different long-acting molecules are currently studied in phase II and III clinical trials, and many others are in stage of early development.<sup>[6]</sup> Only a few of these drugs have already been approved for use as injectable drugs by Food and Drug Administration and the European Medicines Agency and are still not available in Italy on a large scale.<sup>[7]</sup>

The aim of this multicenter cross-sectional study is to evaluate patients' expectations and preferences regarding long-acting antiretroviral agents and their method of administration.

## 2. Material and Methods

We carried out an anonymous online survey between June 1, 2020, and June 30, 2020. The interviews were conducted through Google forms, asking HIV-positive people to judge their relationship with daily cART and to give their opinion about LAI drugs. We also collected data about the age of the patients, the center where they are followed, time passed since the diagnosis, and their compliance to cART. This study was conducted under the Institutional Review Board "Catania 2" approval, protocol number 04/C.E./2018.

The questionnaire was based on a multimethod research divided into 2 parts: an exploratory analysis followed by descriptive analysis.

The first part consisted of semistructured questions to better analyze social-demographic aspects, such as gender, age, occupation, residency and location of their follow-up clinic, year of diagnosis, and pill burden. The second part was useful for understanding the psychological and social impact of HIV infection on patients' life and their adjustment to the diagnosis. In this part, we included ad hoc questions to evaluate patients' interest in LAI rather than oral cART. The survey consists of 22 questions with alternatingly multiple-choice answers (18), multiple-choice answer with the possibility of adding an additional answer (3), and open-ended questions (1).

The complete questionnaire is available in Supplemental Material (Supplemental Digital Content, <http://links.lww.com/MD/H25>).

Twenty-six Italian infectious diseases specialists have contributed to the first phase of the questionnaire distribution, recruiting a maximum of 10 patients each. Later, the same questionnaire was forwarded to HIV patients' organization that distributed it to members through social media.

Statistical analysis was performed with IBM SPSS Statistics version 26.0 for Windows (IBM, Armonk, NY) and GraphPad Prism 8.0 for MacOS (GraphPad Software LLC, San Diego, CA).

Count and percentages were used to summarize categorical variables. Chi-square test was used to test the relationship between variables. Bonferroni adjustment was used to perform post hoc analysis.

Given the small number, male-to-female transgender patients were included in the female population to simplify the statistical analysis.

## 3. Results

### 3.1. Patients

A total of 242 individuals from 26 different Italian HIV outpatient clinics participated. Among them, 58 (24.0%) were females, 182 (75.2%) were males, and 2 (0.8%) were male-to-female

transgender. The youngest patient was included in the 18 to 29 age range, while the oldest was included in the 70 to 79 age range (Fig. 1).

At the moment of answering the survey, 110 (45.5%) of the interviewees were salaried workers, 60 (24.8%) were independent contractors, 8 (3.3%) were students, 34 (14.0%) were unemployed, and 30 (12.4%) were retired.

Eighty-seven (36.0%) patients lived in Northern Italy, 61 (25.2%) in Central Italy, 17 (7%) in Southern Italy, and 77 (31.8%) lived in Sicily or Sardinia. Fifty-seven (23.6%) patients stated that they lived in the countryside or in a village, while 185 (76.4%) lived in a town or a city.

One hundred thirty-two (54.5%) were on follow-up at an HIV outpatient clinic located within their town or city borders, 99 (40.9%) went to a clinic located in the same region but not in their town nor city, and 11 (4.5%) were on follow-up in a different region. Table 1 summarizes patients' characteristics.

### 3.2. Data about HIV infection and treatment

Among the 242 patients, 45 (18.6%) were diagnosed within 5 years, while the majority of the patients (N = 64, 26.4%) had lived with HIV for 10 to 20 years (Fig. 2).

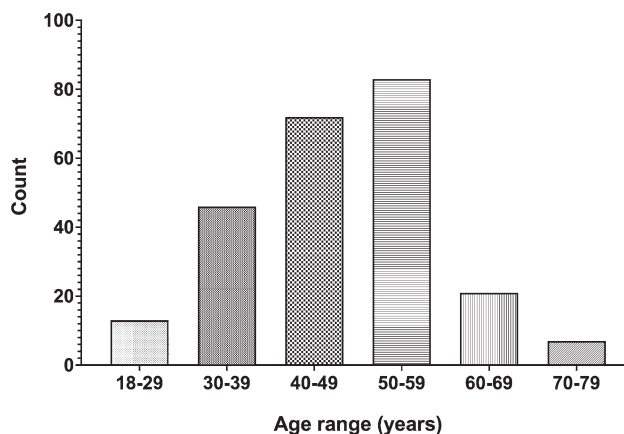
A vast number of interviewees (N = 142, 58.7%) were on a daily STR treatment, 71 (29.3%) were taking 2 pills per day, 18 (7.4%) were taking 3 pills per day, and 11 (4.5%) were taking >3 pills per day.

One hundred thirty-one patients (54.1%) revealed that they are not fully compliant with the treatment in the last 12 months: 61 (25.2%) forgot to take their pills once or twice per year, 36 (14.9%) 3 to 5 times per year, and 9 (3.7%) >3 times per month. Surprisingly, there was no statistically significant difference between adherence ( $P = .076$ ) and number of time the patients missed their therapy ( $P = .070$ ) according to the number of pills in their regimen (Tables S1 and S2, Supplementary Digital Content, <http://links.lww.com/MD/H26>).

About 40% of our population was also taking medication for health conditions not related to HIV infection.

The survey also included 6 questions about patients' feelings toward the disease and their treatment.

The majority of the interviewees (62.8%) said they felt aware of the infection and a few of them (20.2%) felt optimistic. More than 50% of the patients declared to live their life normally



**Figure 1.** The bar graph in this figure shows the distribution of the patients by age. Most of the patients answering the questionnaire were middle-aged (40–59 yr). Thirteen patients (5.4%) were 18–29 yr old; 46 patients (19.0%) were 30–39 yr old; 72 patients (29.8%) were 40–49 yr old; 83 patients (34.3%) were 50–59 yr old; 21 patients (8.7%) were 60–69 yr old; 7 patients (2.9%) were 70–79 yr old.

**Table 1**  
**Patients' characteristics.**

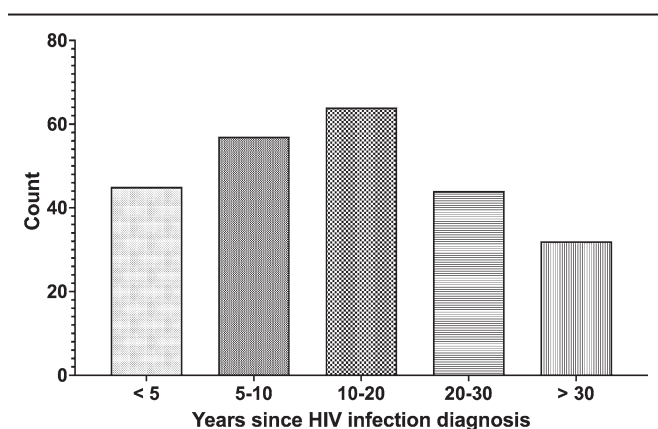
Characteristics	N	%
Sex		
Female	58	24.0
Male	182	75.2
M2F	2	0.8
Occupation		
Salaried workers	110	45.5
Independent contractors	60	24.8
Students	8	3.3
Retired	30	12.4
Unemployed	34	14.0
Place of origin		
Northern Italy	87	36.0
Central Italy	61	25.2
Southern Italy	17	7.0
Sicily/Sardinia	77	31.8
Place of residence		
Countryside/village	57	23.6
Town/city	185	76.4
Clinic location		
Within town/city of residence	132	54.5
Within region of residence	99	40.9
Outside region of residence	11	4.5

M2F = male-to-female transgender.

after the diagnosis and a lower percentage accepted their diagnosis. The largest part of the interviewees (51.2%) stated that the HIV diagnosis compromised their relationships, both steady and occasional ones, and socializing in general.

Fifty-nine percent of the population answered that they have never been discriminated because of the infection. However, 24.5% of the population was discriminated more than once since the diagnosis.

cART stands for safety for the vast majority of the interviewees, and it represents a chance for 23.8%. On the other hand, 10.9% saw the cART as a duty, 3.1% as a life sentence, and an additional 3.1% as a limitation of personal freedom. Finally, we asked the patients to consider the impact of daily cART on everyday life: the number of patients choosing safety and chance decreased in favor of “duty” (18.7%), “restriction of freedom” (6.7%), and “life sentence” (7.3%; Fig. 3).



**Figure 2.** The bar graph in this figure shows the distribution of the patients by time since HIV diagnosis. Forty-five patients (18.6%) had their diagnosis <5 yr before the survey; 57 (23.6%) had their diagnosis 5–10 yr before; 64 (26.4%) had their diagnosis 10 to 20 yr before; 44 (18.2%) had their diagnosis 20 to 30 yr before; 32 patients (13.2%) had their diagnosis >30 yr before.

### 3.3. Knowledge and interest in long-acting drugs

One hundred forty-three (59.1%) patients already knew about long-acting drugs before the survey. Two hundred twenty-nine (94.6%) participants stated that they would be interested in a treatment with a different intake frequency, if available, and 215 (88.8%) also stated that they would immediately agree to change their actual daily regimen for a long-acting one if their attending physician would offer it (Table S3, Supplemental Digital Content, <http://links.lww.com/MD/H27>).

At the end of our survey, we asked the patients if a “hospital-administration only” policy would be a limitation for them, and 35.5% of the patients answered that it would be. Moreover, 140 patients (57.9%) answered they would rather have the injectable treatment administered at their home (Fig. 4).

### 3.4. Statistical analysis

Combining patients' characteristics and their relationship with the HIV infection and cART, we tried to figure out if there were some features recurring in patients who are more eagerly waiting for the long-acting drugs.

The female patients included in this study are less compliant to treatment ( $P = .005$ ) and forget their treatment more frequently ( $P = .022$ ) than males. Female patients are also less informed about long-acting drugs ( $P = .015$ ), less interested in them ( $P = .018$ ) and they consider an “hospital-administration only” policy an obstacle more often than men ( $P = .020$ ).

Patients younger than 50 years were more informed about long-acting drugs ( $P = .013$ ) and their knowledge about long-acting drugs was higher if patients had a job ( $P = .001$ ), lived in a city or town ( $P = .001$ ), or received their HIV infection diagnosis <10 years before answering this survey ( $P = .025$ ). A “hospital-administration only” policy would make people not living in a city or town less interested in long-acting drugs ( $P = .007$ ).

There are no significant differences in either knowledge ( $P = .690$ ) or interest ( $P = .676$ ) in long-acting drugs with regard to the location of the HIV outpatient clinic the patients were followed at.

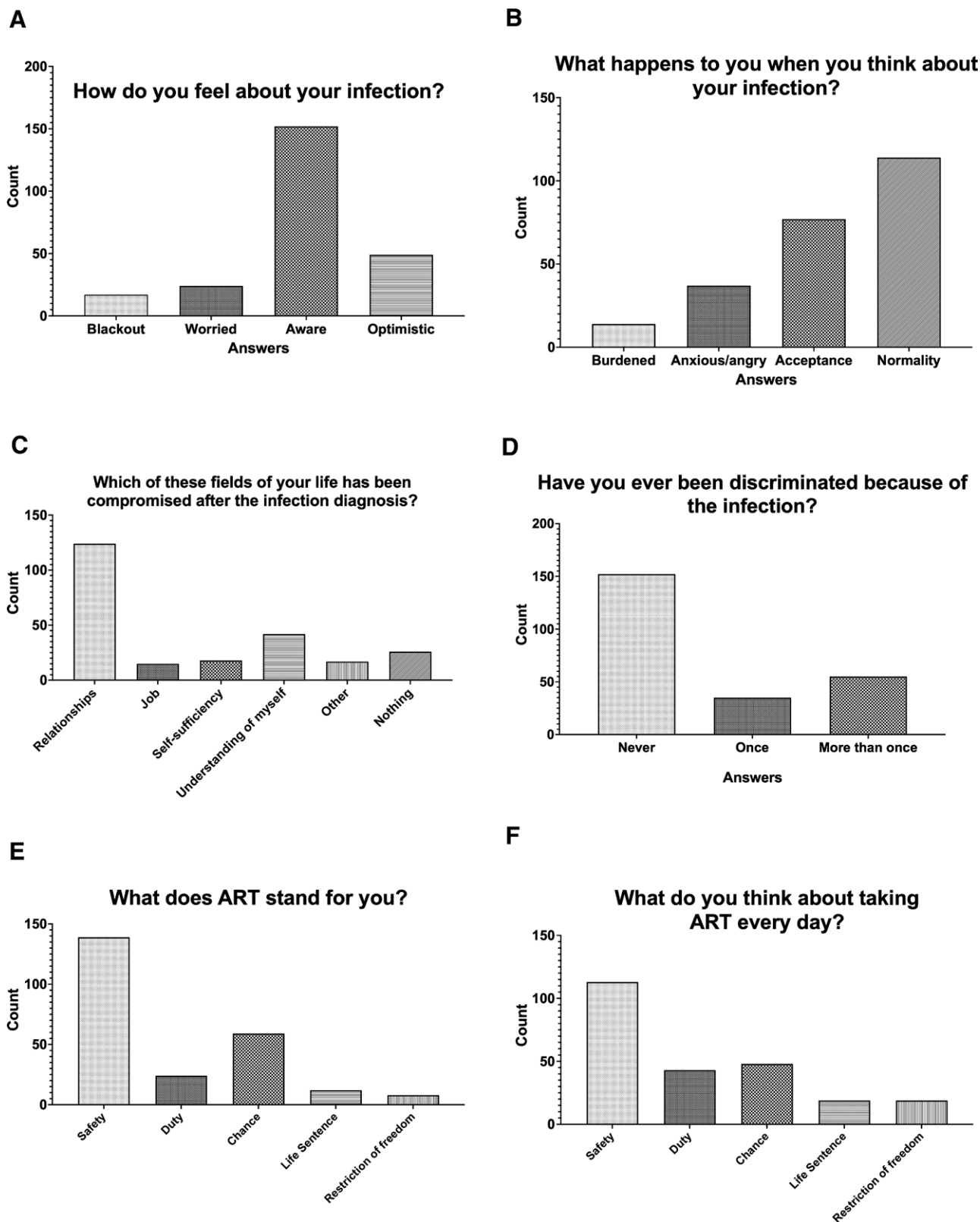
Surprisingly, there was no difference in patients' knowledge ( $P = .841$ ) and interest ( $P = .390$ ) in LAIs according to the number of pills in their regimen (Tables S4 and S5, Supplemental Digital Content, <http://links.lww.com/MD/H28>).

## 4. Discussion

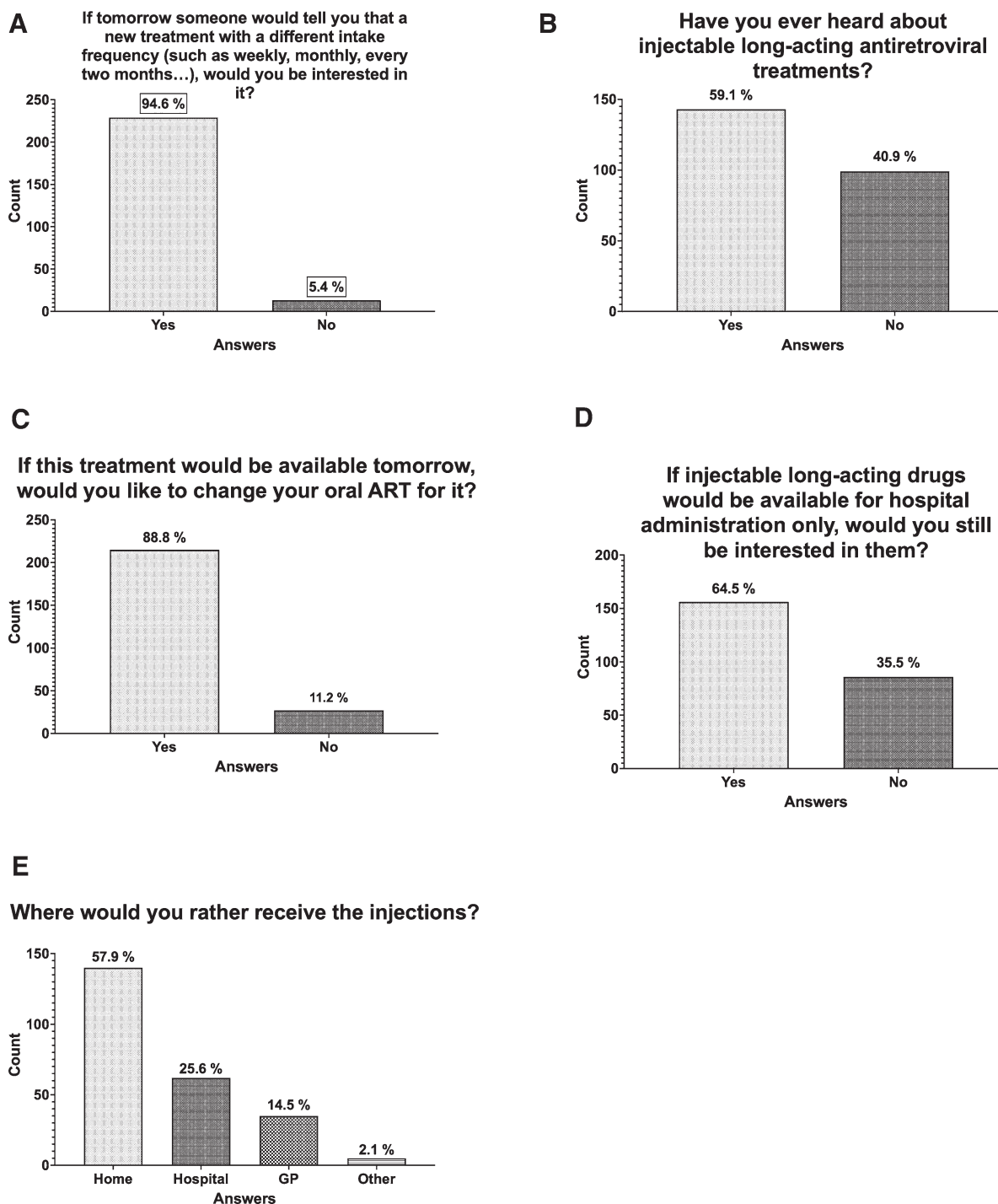
According to literature, LAI therapy appears to give numerous advantages in HIV treatment and prevention, innovating both pharmacologic research and patients' quality of life.<sup>[7–9]</sup> LAI diffusion may mitigate a vast number of the challenges faced by PLWH. In fact, as shown by this study, daily cART is perceived as a source of security by many, but its daily intake also represents a limit and a burden to many others.

One of the results that stand out in our analysis is the high number of unemployed patients. Even if these data may not imply the effective absence of occupation due to the high rate of undeclared work in our country, it may also display the patient's reluctance to approach the work world because of the possibility of discrimination. Aside from the important psychological aspects bringing out what it means living with HIV and how stigma and discrimination are a constant in PLWH life, we were able to observe patients' inclination toward health-related mobility, especially in patients living in the islands and in Southern Italy who prefer to be in follow-up at clinics scattered throughout national territory.

This phenomenon indicates 2 main elements: one is related to the greatest number of highly specialized health facilities in Northern Italy or in big cities and the other to the personal causes



**Figure 3.** This figure shows the frequency of the answers to questions 10 to 15 of the survey (Supplemental Material, Supplemental Digital Content, <http://links.lww.com/MD/H25>). It is shown that (A) 152 (62.8%) patients say they are aware about their infection; (B) 114 (47.1%) patients does not feel in a particular way when they think about their infection; (C) 124 (51.2%) patients think that their relationships with those around them were affected by the diagnosis; (D) while 152 (62.8%) patients say they were never discriminated because of the infection, 35 (14.5%) and 55 (22.7%) felt discriminated because of the infection once or more than once, respectively; (E) for the majority of the patients interviewed, cART represents safety (57.4%) or a chance (24.4%); but when asking the interviewees what they think about taking ART daily, 43 of them (17.8%) say that it is a duty.



**Figure 4.** This figure shows how the patients answered the final 5 questions of the survey (Supplemental Material, Supplemental Digital Content, <http://links.lww.com/MD/H25>).

of mobility. For example, some interviewees who move to another city or region for non-HIV-related causes sometimes prefer to rely on clinicians in their hometown or region fearing the possibility of others discovering their condition. Similarly, many PLWH who do not need to move to choose to access care away from home.

We were surprised to detect that such a high number of PLWH assuming a STR were ready to switch to bimonthly injections. Moving from this consideration, STR probably could not more represent the top condition for all patients. We found no difference either in interest or knowledge of LAIs among groups of patients taking different number of pills. Moreover, even though PLWH included in this survey have a good relationship with

cART, understanding its importance for their safety, they also feel that taking a pill daily is a burden and a constant reminder of their condition.

In fact, a psychological advantage of switching to LAI is associated with the reduction of total pills amount. At the moment, PLWH are estimated to take an average of 1 pill per day for at least 40 years. This means 14,610 pills over 480 or 240 (if bimonthly) injections. It would represent a reduction of effective day of treatment of over 96% (if administered monthly) and 98% (if bimonthly).<sup>[8]</sup>

The patients' compliance to treatment will also benefit from the reduction of days of active treatment. In fact, in our survey,

more than half of the patients revealed that they missed 1 or more days of administration during the previous year. A vast number of patients forgetting pills, also declared they experienced discrimination at least once since the HIV diagnosis. However, our post hoc analysis showed no significant correlation between stigma and poor adherence.

Current cART regimens can tolerate a higher number of consecutive missed doses than the previous molecules; however, patients' adherence to therapy can be variable during lifetime and cART forgiveness may not be enough if the number of consecutive missed doses is too high.<sup>[5]</sup> LAIs represent a possible solution avoiding daily administration and reducing the risk of virologic rebound and development of drug resistance possibly leading to the onset of HIV-related diseases.

The innovative character of LAI cART may represent an exciting advancement in HIV treatment, leading the way to numerous "firsts" in HIV therapy history: for the first time a long-acting therapy has been introduced in this field; for the first time patient-reported outcome on-going have been introduced during the initial phase of drug development; for the first time a therapy has been approved both for treatment and prevention showing such high superiority in prevention despite the previous molecules that clinical trials were ended earlier.<sup>[7,10]</sup>

Participants highlighted LAI cART as a highly desirable treatment option and a such high number of patients showed an enthusiastic response to the opportunity to be treated directly at home.

Patients' health-related migration could interfere with access to LAI therapy in case of an exclusive in-hospital administration. As shown in our results, a hospital administration policy may be a limit for elder or fragile patients or for PLWH living far from their outpatient clinic.

The possibility of alternative ways as home administration should be considered in order to overcome access to care challenges, even for the patients who prefer to travel to other cities or regions to be treated in secret.

The introduction of LAI in everyday clinical practice will inevitably lead to a reorganization of the National Health System. If just 20% of the approximately 150,000 PLWH undergoing oral cART in Italy at the moment will be switched to LAI in the next 2 years, we will need to guarantee 360,000 intramuscular injection per year. It seems clear that the current model of therapy dispensation, even if it differs from one center to another, will not be efficient enough and may not use the contribution of local and hospital pharmacies. Therefore, the LAI hospital administration may require a complete reorganization of spaces and personnel involved.

During the last 2 years, the coronavirus disease 2019 pandemic forced a fast shift from regular ambulatory and hospital activity towards telemedicine and e-health. Because of the situation, a normally difficult and slow process of change is now easily implemented and accessible to all.

Especially at this time, the possibility of treating patients directly at home or in other nonhospital settings should be considered as a valid option. Both the National Health System and the patients would benefit from this possibility: the load on outpatients' clinic would be reduced and all the patients could easily access the therapy.

Our study has some limitations, such as we do not know how many people saw the survey through social media and passed the chance to reply or those who were actively offered to answer and refused; therefore, we do not know anything about possible passive selection bias. However, there is no active selection bias, as we did not ask the patients what they thought about long-acting drugs before the survey.

On the basis of these results, we decided to further investigate the economic aspects of LAI use in terms of consumer attitude, cost-minimization, cost-effectiveness, cost-benefit, and cost-utility. Said analysis will be published once the study is complete.

In conclusion, the data emerging from our survey reveal that around 90% of PLWH are interested in changing their actual treatment with a long-acting one. Moreover, a high number of patients showed an enthusiastic response to the new opportunity to be treated directly at home. The introduction of these new drugs could be revolutionary and represents an important step towards treatment simplification.

## Acknowledgments

The LAI Survey Group: Diego Ripamonti, ASST Papa Giovanni XXIII, Infectious Diseases, Bergamo, Italy; Salvatore Martini & Paolo Maggi, Università della Campania "L. Vanvitelli", Unit of Infectious Diseases, Napoli, Italy; Cristina Gervasoni & Amedeo Capetti, ASST Sacco Hospital, Unit of Infectious Diseases, Milano, Italy; Chiara Dentone, Ospedale S. Martino Genova, Infectious Diseases, Genova, Italy; Giovanni Cenderello, Sanremo Hospital, Unit of Infectious Diseases, Sanremo, Italy; Andrea Calcagno, Ospedale Amedeo di Savoia, Unit of Infectious Diseases, Torino, Italy; Giancarlo Orofino, ASL Città della Salute, Unit of Infectious Diseases, Torino, Italy; Annamaria Cattelan, Azienda Ospedaliera di Padova, Unit of Infectious Diseases, Padova, Italy; Evelina Tacconelli, University of Verona, Department of Diagnostics and Public Health, Verona, Italy; Francesca Vichi, USL Firenze Centro, Unit of Infectious Diseases, Firenze, Italy; Annalisa Saracino, Policlinico di Bari, Unit of Infectious Diseases, Bari, Italy; Sergio Lo Caputo, Università di Foggia, Department of Clinical and Experimental Medicine, Foggia, Italy; Giovanni De Socio, AOU Perugia, Unit of Infectious Diseases, Perugia, Italy; Giuliana Guadagnino, AO di Cosenza, Unit of Infectious Diseases, Cosenza, Italy; Giustino Parruti Azienda USL di Pescara, Unit of Infectious Diseases, Pescara, Italy; Marco Borderi, Policlinico S. Orsola Malpighi, Unit of Infectious Diseases, Bologna, Italy; Cristina Mussini, Policlinico Modena, Unit of Infectious Diseases, Modena, Italy; Gabriella D'Etterre, Policlinico Umberto I, Unit of Infectious Diseases, Roma, Italy; Tiziana Quirino, Fondazione ASIA, Milano, Italy; Giordano Madeddu, University of Sassari, Medical Surgical and Experimental Sciences, Sassari, Italy; Antonio Di Biagio, IRCCS AOU S. Martino, Unit of Infectious Diseases, Genova, Italy.

## Authors contributions

**Conceptualization:** Marta Celesia, Benedetto Maurizio Celesia, Alessandra Tzannis

**Data curation:** Marta Celesia, Michele Trezzi, Emanuele Focà, Margherita Errico, Paola Cinque, Silvia Nozza, Antonella Cingolani

**Formal Analysis:** Manuela Ceccarelli, Marta Celesia

**Methodology:** Marta Celesia, Benedetto Maurizio Celesia, Alessandra Tzannis, Manuela Ceccarelli

**Project administration:** Benedetto Maurizio Celesia

**Writing – Original Draft:** Marta Celesia, Vittoria Moscat, Manuela Ceccarelli

**Writing – review & editing:** Manuela Ceccarelli, Benedetto Maurizio Celesia

## References

- [1] Gallo RC. A reflection on HIV/AIDS research after 25 years. *Retrovirology*. 2006;3:72.
- [2] European Centre for Disease Prevention and Control. HIV/AIDS surveillance in Europe. 2020. Available at: <https://www.ecdc.europa.eu/sites/default/files/documents/hiv-surveillance-report-2020.pdf>. [access date 13 May, 2021].
- [3] Altice F, Evarherhe O, Shina S, et al. Adherence to HIV treatment regimens: systematic literature review and meta-analysis. *Patient Prefer Adherence*. 2019;13:475–90.
- [4] Cambou MC, Landovitz RJ. Novel antiretroviral agents. *Curr HIV/AIDS Rep*. 2020;17:118–24.

- [5] Mulato A, Acosta R, Chang S, et al. Simulating HIV breakthrough and resistance development during variable adherence to antiretroviral treatment. *J Acquir Immune Defic Syndr*. 2021;86:369–77.
- [6] clinicaltrials.gov. ClinicalTrials.gov. Available at: <https://clinicaltrials.gov/ct2/results?cond=HIV+Infections&term=long-acting&country=&state=&city=&dist=>. [access date 13 May, 2021].
- [7] Overton ET, Richmond G, Rizzardini G, et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study. *Lancet*. 2020;396:1994–2005.
- [8] Kerrigan D, Murray M, Sanchez Karver T, et al. Feasibility of implementing long-acting injectable anti-retroviral therapy to treat HIV: a survey of health providers from the 13 countries participating in the ATLAS-2M trial. *AIDS Res Hum Retroviruses*. 2021;37:207–213
- [9] Koren DE, Fedkiv V, Zhao H, et al. Perceptions of long-acting injectable antiretroviral treatment regimens in a United States urban academic medical center. *J Int Assoc Provid AIDS Care*. 2020;19:2325958220981265.
- [10] Flexner C, Owen A, Siccardi M, et al. Long-acting drugs and formulations for the treatment and prevention of HIV infection. *Int J Antimicrob Agents*. 2020;57:106220.