

**Awareness and perception of accuracy of the Undetectable=Untransmittable message (U=U) in Italy: results from a survey among PLWHA, infectious-diseases physicians and people having unprotected sex.**

**Key words: Undetectable, untransmittable, U=U, awareness, accuracy, HIV.**

**Running title: U=U awareness and perception of accuracy in Italy.**

## **Abstract**

Accumulating evidence on absence of risk of sexual transmission of HIV by persons living with HIV/AIDS (PLWHA) with undetectable plasma HIV-RNA (HIV-RNA <200 copies/ml), led to the worldwide campaign “U = U” (undetectable = untransmittable). Purpose of this study was to evaluate the perceived accuracy of this message among PLWHA, HIV-negative people having unprotected sex (PHUS) and infectious diseases (ID) physicians in Italy, in order to inform subsequent specific efforts and implementation of HIV prevention strategies. A nationwide survey has been conducted in clinical centers, community-based voluntary test&counselling centers (CBVTC) and through fast-track cities websites using three different anonymous questionnaires (for ID physicians, for PLWHA and for PHUS) .

1121 participant filled the questionnaires: 397 PLWHA; 90 physicians; 634 PHUS. Awareness of U=U message has been reported in 74%, 92% and 47% of PLWHA, ID physicians and PHUS, respectively. The perception of accuracy of U=U message among those aware was reported as high in 80.4%, 79.5%, and 67.3% of PLWHA, ID physicians, and PHUS respectively.

Physicians perceived that 11% of PLWHA have a high rate of perception of U=U, whereas among PLWHA, only 34% reported definitive positive messages from physicians. Discrepancies between awareness and perception of accuracy of the message U=U in PLWHA and physicians have been found, suggesting a still low confidence in the community regarding the message itself.

## **Introduction**

The efficacy of highly effective combination antiretroviral therapy (ART) on HIV transmission has been widely demonstrated in observational studies (Attia et al, 2009; Das et al, 2010). No single incident HIV infection linked to the main partner, despite high rates of condomless sex, was definitively reported among participant of HTPN 052 (Eshleman et al, 2017), PARTNER study (Rodger et al, 2016), and to Opposite Attract study (Bavinton et al, 2014; Grulich et al, 2015).

As a consequence, the Prevention Access Campaign has been set up to spread the slogan “Undetectable = Untransmittable” (commonly referred in social media as #UequalsU) with the purpose of raising HIV prevention awareness and reducing HIV stigma (Prevention Access Campaign, 2016).

However, the success of the message is directly dependent on its dissemination and awareness firstly among all the people who can benefit from it, i.e. not only people living with HIV, but also health professionals and people at risk of contracting HIV. At present, available evidence suggest a low level of awareness of the message among those involved (Card et al, 2018; Carter et al, 2015; Holt et al 2016; Terrence Higgins Trust, 2017).

Since the mode of spreading of the message U=U to PLWH is multifactorial, physicians' belief in the accuracy of the message represents a fundamental step for the dissemination of the message itself, but it is still far from being realized. In the same way for PLWH and people vulnerable to acquire it, knowing, discerning and accepting the U=U message are first key steps for impact the personal and public views of HIV infection and break down the HIV stigma.

The objective of this study is to assess the level of awareness of the U=U message in Italy in populations involved at different levels in the dissemination and reception of the U=U message (PLWH, people at risk of acquiring HIV and Infectious Diseases (ID) doctors) and to identify the characteristics of each group that could limit the dissemination and application of the message.

## **Methods**

### Data Source

Between January and July 2020, an anonymous nationwide web survey was conducted in three different target groups in Italy. Group-1: PLWH followed in the clinical centers participating in the ICONA Foundation Study (ICONA); Group-2: ID physicians from clinical centers afferent participating in ICONA; Group-3: HIV-uninfected people having unprotected sex (PHUS) who had had access to Community-based voluntary test& counselling centers (CBVTC) or visiting websites of fast track cities in Italy (Bergamo and Milan).

The Icona Foundation Study is an Italian cohort of patients with HIV, an extension of the original ICONA study (described elsewhere) (d'Arminio Monforte et al, 2000).

Participants were invited through the distribution of information brochures distributed in Icona Foundation clinical centres and through social media. Access to the survey was via the website [www.uequalsuicona.it](http://www.uequalsuicona.it) or with a specific QR code. The survey has been released only in Italian. Upon beginning the survey, participants were informed that the survey would take approximately 10 minutes and a brief online consent form has been presented.

### Measures

The entire survey has been developed, within a working group of members of the Icona Foundation Scientific Committee and Community Advisory Board, using previous works (Rendina et al, 2018) as model.

Three different anonymous questionnaires for ID physicians, PLWH and PHUS were set up and are briefly described below and in Table 1 (the complete survey is included as Supplementary File).

#### *U=U measures of knowledge and accuracy for ID physicians, PLWH and PHUS*

All participants in the 3 groups were asked, "Have you heard of the statement U=U?" with a binary answer (yes/no). In case of positive answer, other question regarding U=U were asked, among

those, one was on the perceived accuracy of U=U, adapted from the Rendina et al. 2018 work, “How accurate do you feel the concept is” responses were collected on a Likert scale from 1 (=completely inaccurate) to 4 (=completely accurate).

#### *Other U=U measures for ID physicians, PLWH and PHUS*

ID physician aware of U=U responded also on the some questions regarding the communication strategy to PLWH of U=U, and whether they think that PLWH have understood the meaning of U=U with responses on a Likert scale from 1 (=not at all) to 4 (=very).

For all the PLWH and PHUS –regardless of the reported knowledge of U=U– the following question has been asked “How would you assess the risk of HIV transmission to a sexual partner in a person with HIV on treatment and an undetectable viral load?” (High/Low/Very Low/Absent).

For this two groups, other questions through which means of communication they acquired the information on U=U and in detail the communications of U=U by their ID physician only for PLWH have been collected. The last set of questions for PLWH explored how U=U had impacted on their personal life asking for changes in their sexual/affective life, changes in their perceived stigma/discrimination for their HIV status, changes in their habits, the difficulties to accept the U=U message for partners, family, friends and other healthcare workers. Finally for PHUS the following question has been asked “How much U=U change your sexual/affective activity towards a possible HIV+ partner?” with again responses on a Likert scale from 1 (=not at all) to 4(=very).

#### *Statistical Analysis*

Sociodemographic, behavioural and clinical characteristics as well as the other relevant responses to the survey in the three groups (ID physician, PLWH, PHUS) have been initially described using absolute and relative frequencies, without performing a formal comparison between the groups.

Logistic regression models have been fitted to investigate factors associated with the binary outcomes ‘awareness of U=U’ (Yes vs No). Due to the right skewed distribution of response for the variable ‘accuracy of U=U’, this ordinal endpoint has been dichotomized as ‘U=U completely

accurate' vs 'other responses' and binary logistic regression models have been fitted to investigate the factors associated with a perceived high accuracy of U=U among users who were aware of U=U separately for each group. We then conducted multivariable, logistic regression models to explore factors associated both with awareness and accuracy of U=U. The socio-demographic, clinical and behavioural variables retained in the adjusted model have been chosen according to significance in the crude analysis and according to previous studies (Rendina HJ et al. [JIADS 2018](#), Rendina HJ et al. [JAIDS 2020](#), Torres TS et al. [JIAS 2020](#)). Multivariable models have been fitted only for PLWH and PHUS, not for ID physicians group, due to the small sample size. In order to assess the representativeness of the sample, a comparison was made regarding sociodemographic characteristics with the patients included in the ICONA cohort, followed in same period and at the same clinical centers of patients responded to the survey. As a consequence of this, to reduce the collider bias, typical of the non-randomly samples of voluntary web-based surveys education level and sexual orientation were not included as variables in the regression analysis in the analyses of the PLWH subgroup.

The perception of the U=U message, seen as composite endpoint of awareness of U=U with a recognized high accuracy of the message, has been compared between PLWH and ID physician of the same centers to verify among the 4 centers with higher number of responses (at least 10 PLWH and 10 ID physician per center) the consistency on perceived accuracy between ID physician and their patients. Analyses have been conducted using Stata v.14, setting a  $p < 0.05$  as threshold for statistical significance.

### Ethics

This study is an extension of the Icona Foundation study approved by the institutional review boards of all the participating centers. An informed consent has been obtained from the participants to process their anonymous data collected within the survey and use it for the study.

## Results

A total of 1488 users started the survey, 30 did not accept the informed consent to data processing and study participation and has been excluded, 118 drop immediately the survey after the consent without indicating the group, 48 ID physician, 85 PLWHA and 85 PHUS did not complete and have been excluded. 1121 participants completed the questionnaires and were evaluable for analysis. Socio-demographic characteristics are reported in Table 2. Among the 397 PLWH, mostly Italian, 81.6% were male, 67.0% were gay, bisexual and other man who had sex with other man (GBMSM). 95.4% of the PLWH declared to have undetectable HIV-RNA and 38.8% had a stable HIV-neg sexual partner

With regard to PHUS, they were mostly young (72.7% < 40 years), males (68.0%), GBMSM (64.6%), mostly reflecting the population of CTCs and fast track cities websites in Italy. With regard to the ID physicians who responded were predominantly young (54.4% < 40 years), 81% are involved in management of HIV patients with relatively limited experience both in terms of time (53% <10 years) and PLWH in care (49% < 100 PLWH).

In order to reduce the collider bias of the potential associations, a comparative assessment was made between patients enrolled in ICONA and those responding to the survey followed in the same calendar period of the survey and in the same clinical centres (see supplementary Table 1s). PLWH who responded to the survey were more frequently Italian (94% vs 83%,  $p < 0.001$ ), GBMSM (61% vs 46%,  $p < 0.001$ ), with higher level of education (university 39% vs 13%,  $p < 0.001$ ), longer time since HIV diagnosis (47% vs 31% had been diagnosed for more than 10 years,  $p < 0.001$ ), longer time on ART (47% vs 31% had been on ART for more than 10 years,  $p < 0.001$ ), while no significant differences were observed with regard to age, sex and Italian geographical area.

*Awareness and perception of accuracy of U=U message*

As shown in Table 2, the awareness of U=U was reported in 74.6%, 92.2% and 46.8% of PLWH, ID physicians and PHUS respectively. Eighty-three percent of ID physicians reported to spend a relevant time (very/enough) speaking about U=U during visit, and 81% of them reported good patient understanding of the concept.

Among the three groups of participants, the perception of accuracy of U=U message was reported as completely accurate in 80.4%, 79.5%, and 67.3% of PLWHA, ID physicians, and PHUS respectively.

Looking at how the U=U message might modify behaviors and attitudes, PLWH reported an improvement in their sexual lives in 71.6% of cases, whilst 56.7% perceived a reduction of HIV-related stigma. Eighty-two percent of ID physicians did not report a change in the prescribed frequency of HIV-RNA monitoring as a consequence of spreading of U=U message.

On the other hand, 43.6% of PLWH reported to have received information on U=U from ID physicians, but only 33% reported to be completely assured about having unprotected sex if HIV-RNA undetectable.

#### *Factors associated with awareness of U=U*

In Table 3, factors associated with awareness of U=U message are shown for three groups of respondents after fitting separate logistic regression models.

Among PLWH, age (40-50 years old vs <40 years old, AOR 0.46, 95%CI 0.24-0.89) was independently associated with a lower awareness of U=U message, whilst to be male (AOR 2.42, 95%CI 1.30-4.50), to be on cART for 5-10 years (vs < 5 years, AOR 2.62, 95%CI 1.30-5.28) and to be treated in a southern Italy clinical center (vs Central, AOR 2.57, 95%CI 1.03-6.39) were associated with a higher awareness.

Among physicians, the only factor associated with a higher awareness of U=U was to be involved in the care of PLWH (OR 14.8, 95%CI 2.57-85.1).



Factors associated with awareness in PHUS were age (40-50 years old vs <40 years old, AOR 4.51, 95%CI 2.69-7.57), level of education (secondary/college vs University, AOR 0.49, 95%CI 0.33-0.71), time from last HIV test (>1 year vs <6 months, AOR 0.37, 95%CI 0.22-0.60) and the number of sexual partners (>50 in the last year vs 0, AOR 3.52, 95%CI 1.14-10.86).

#### *Factors associated with perception of accuracy of U=U*

Table 4 shows factors associated with a perception of accuracy of the U=U message reported as high (“completely accurate”). Among participants who reported to have received information regarding U=U, to have received information inside hospital (AOR 2.09; 95%CI 1.03-4.24) was the only factor associated with high perception of accuracy in PLWHA.

In PHUS, a lower level of education has been reported to be associated also with a lower probability of perception of high accuracy of U=U (AOR 0.54, 95%CI 0.29-0.98). In contrast, having received information about U=U in the community setting for PHUS (AOR 2.80, 95%CI 1.50-5.23,  $p=0.001$ ) and have a stable partner with HIV infection (AOR 3.83, 95%CI 1.00-16.71) were associated with perception of higher accuracy of the message.

The concordance between doctor's and patient's perception of accuracy of the U=U message was investigated in the 4 centres that included the largest number of doctors and patients from the same centre in the survey (“intracenter accuracy of perception”). In 2 out of 4 centres a significantly higher perception of accuracy was observed in physicians than in patients (Center 2 90% vs 48%,  $p=0.021$  and Center 3 100% vs 50%,  $p=0.004$ ) (Figure 1).

## **Discussion**

The results of the present study, the first in Italy carried out at national level after the launch of the U=U campaign, show a wide variability in the level of awareness of the U=U message in the selected population responding to the survey. In particular, 75% of PLWH, 92% of ID physicians belonging to the same clinical centers of recruited PLWH, but only 47% of HIV-negative people at high risk of infection declared to be aware that an HIV-infected person does not transmit the virus to his/her sexual partner if he/she has undetectable HIV-RNA in the plasma. In addition, the perception of a high accuracy of U=U message, among those subjects aware of U=U, was reported in 79.5%, 80.4% and 67.3% of ID physicians, PLWHA and PHUS respectively. However, the penetration of U=U message in the doctor-patient relationship, is not yet sufficient, given that 84.5% of ID physicians reported to spend a relevant time during periodical visit speaking about U=U, with 60.6% of them reported good patient understanding of the concept, but from the PLWH's perspective, only 48.7% reported to have received information on U=U from ID physicians. And, of them, only 33.0% reported to be completely assured about having unprotected sex if HIV-RNA undetectable.

Moreover, looking at how the positive perception of U=U could have modified behaviors and attitudes, PLWH reported an improvement in their sexual lives in 71.6% of cases, but approximately only a half perceived a reduction of HIV-related stigma.

In our survey, the low prevalence of PLWHA perceiving a reduction of HIV-related stigma due to U=U (57%) suggests that the level of discussion about U=U between PLWH and their treating physician is still insufficient to ensure the application of the message in everyday life.

The survey on PLWH was conducted on individuals who volunteered to participate thus, as reported for other voluntary web surveys, it is possible that people with a higher level of culture and who are more likely to express opinions on topics they know are overrepresented. Nevertheless, the patients in the survey are comparable for age and gender to the patients enrolled in ICONA (more than 50 clinical centers involved, for a total of 9000 PLWH in active follow up in Italy), while they

differ in aspects related to time spent with HIV (more years since diagnosis and more years on ART) which do not necessarily indicate collider bias.

Similarly, the sample of HIV-negative people at high risk of HIV transmission can be considered selected since the recruitment, as users of Community network and fast track cities websites were included. Nevertheless, they are among the most important targets on which to plan and focus targeted interventions, so it is essential that the U=U message is disseminated and penetrates precisely among these types of users.

The representativeness of the group of responding physicians, mostly represented by young physicians with not much experience in the care of people with HIV, can be considered limited; but certainly the importance of having had information from this group lies in the opportunity that such a survey may serve as a background for teaching and communication strategies with the new generations of ID physicians. Even though ID physicians are the first and main contact for PLWH in HIV-care, and could deeply influence how the message is conveyed and received, nevertheless, investigating the dissemination and the perception of U=U in the other medical specialties in contact with PLWH, could represent a future research of the cohort.

To date, a limited number of studies analyzed the level of confidence of U=U message across the different communities of PLWH. In particular, in a sample of Australian PLWH responding to a web survey, 70.5% of participants agreed with the general U=U message, but only 48.2% were confident in U=U as an effective HIV transmission prevention strategy across sexual situations, with lack of confidence in U=U more pronounced in minority group participants (Huntingdon et al 2020). We cannot explore the confidence of the message in minorities and in PLWH with lower education, nevertheless the association between low education and low confidence in the accuracy of U=U message in the PHUS, suggests the importance of exploring such aspects also in PLWH communities more difficult to reach by community or social media-based campaigns.

In a nationwide survey of GBMSM in the USA, factors associated with a high perception of accuracy of U=U were undetectable HIV-RNA, a AIDS diagnosis, and lower concern about sexually transmitted infection (Carneiro et al, 2020). In contrast, our survey, did not report any association with HIV-RNA undetectability and perception of accuracy of U=U message (data not shown), probably due to the high level of undetectable plasma viral load (95%) reported by PLWH. A significantly high amount of papers have been published regarding the confidence of U=U message among HIV-negative at high sexual risky behaviors. In a national internet-based cohort of HIV-negative cis men, trans men and trans women who have sex with men in the USA, 85.5% of participants reported having heard of U=U, among those aware of U=U, 42.3% indicated they trusted it. In our study, a lower proportion of PHUS were aware of U=U message, but almost all of those who were aware of U=U reported to have trust in the accuracy of the message (67% completely accurate). Even if with a direct question if “U=U changed their sexual/affective activity towards HIV+ partner”, the confidence in the U=U message, seems lower (29% totally changed). A previous web-based Brazilian survey (Torres et al, 2020) showed that among general HIV-negative population 11% of respondent did not know the what “undetectable” means similar results were also reported by Rendina and colleagues (Rendina et al. 2018). We did not investigate this in our survey, asking only for the knowledge “Undetectable=Untransmissible”.

In conclusion, the present study showed some inconsistency between awareness and perception of accuracy of the message U=U in PLWH and physicians suggesting that there is still low confidence in the community regarding the message itself. More efforts should be implemented to spread the U=U message among subgroups who might benefit from targeted educational campaigns. The results of the present study suggest how even in Italy the dissemination of the U=U concept is still far from being universal and adequate (Bor et al, 2021). Dissemination of the message among PHUS is far from being efficaciously implemented and should represent a priority for increasing knowledge, decreasing HIV stigma and increase access to HIV diagnosis. The involvement of

community-based out-of-hospital structures that on the one hand spread and make the U=U message known in the general population and on the other hand cooperate in making the message penetrate in the everyday life of PLWH is recommended.

## **Acknowledgments**

*Icona Foundation Study Group.* Board of Directors: A. d'Arminio Monforte (President), A. Antinori (Vice-President), M. Andreoni, A. Castagna, F. Castelli, R. Cauda, G. Di Perri, M. Galli, R. Iardino, G. Ippolito, A. Lazzarin, G.C. Marchetti, G. Rezza, F. von Schloesser, P. Viale. Scientific Secretary: A. d'Arminio Monforte, A. Antinori, A. Castagna, F. Ceccherini-Silberstein, A. Cozzi-Lepri, E. Girardi, A. Gori, S. Lo Caputo, F. Maggiolo, C. Mussini, M. Puoti, C.F. Perno. Steering Committee: A. Antinori, F. Bai, A. Bandera, S. Bonora, M. Borderi, A. Calcagno, M.R. Capobianchi, A. Castagna, F. Ceccherini-Silberstein, S. Cicalini, A. Cingolani, P. Cinque, A. Cozzi-Lepri, A. d'Arminio Monforte, A. Di Biagio, R. Gagliardini, E. Girardi, N. Gianotti, A. Gori, G. Guaraldi, G. Lapadula, M. Lichtner, A. Lai, S. Lo Caputo, G. Madeddu, F. Maggiolo, G. Marchetti, E. Merlini, C. Mussini, S. Nozza, C.F. Perno, S. Piconi, C. Pinnetti, M. Puoti, E. Quiros Roldan, R. Rossotti, S. Rusconi, M.M. Santoro, A. Saracino, L. Sarmati, V. Spagnuolo, V. Svicher, L. Taramasso. Statistical and Monitoring Team: A. Cozzi-Lepri, I. Fanti, L. Galli, P. Lorenzini, A. Rodanó, M. Macchia, A. Tavelli. Community Advisory Board: A. Bove, A. Camposeragna, M. Errico, M. Manfredini, A. Perziano, V. Calvino. Biological Bank INMI: F. Carletti, S. Carrara, A. Di Caro, S. Graziano, F. Petroni, G. Prota, S. Truffa. Participating Physicians and Centers: Italy: A. Giacometti, A. Costantini, V. Barocci (Ancona); G. Angarano, L. Monno, E. Milano (Bari); F. Maggiolo, C. Suardi (Bergamo); P. Viale, V. Donati, G. Verucchi (Bologna); F. Castelnuovo, C.

Minardi, E. Quiros Roldan (Brescia); B. Menzaghi, C. Abeli (Busto Arsizio); L. Chessa, F. Pes (Cagliarti); B. Cacopardo, B. Celesia (Catania); J. Vecchiet, K. Falasca (Chieti); A. Pan, S. Lorenzotti (Cremona); L. Sighinolfi, D. Segala (Ferrara); P. Blanc, F. Vichi (Firenze); G. Cassola, M. Bassetti, A. Alessandrini, N. Bobbio, G. Mazzarello (Genova); M. Lichtner, L. Fondaco (Latina); P. Bonfanti, C. Molteni (Lecco); A. Chiodera, P. Milini (Macerata); G. Nunnari, G. Pellicanò (Messina); A. d'Arminio Monforte, M. Galli, A. Lazzarin, G. Rizzardini, M. Puoti, A. Castagna, E.S. Cannizzo, M.C. Moioli, R. Piolini, D. Bernacchia, A. Poli, C. Tincati (Milano); C. Mussini, C. Puzzolante (Modena); C. Migliorino, G. Lapadula (Monza); V. Sangiovanni, G. Borgia, V. Esposito, G. Di Flumeri, I. Gentile, V. Rizzo (Napoli); A.M. Cattelan, G. Parruti, F. Sozio (Pescara); C. Lazzaretti, R. Corsini (Reggio Emilia); M. Andreoni, A. Antinori, R. Cauda, A. Cristaudo, V. Vullo, R. Acinapura, S. Lamonica, M. Capozzi, A. Mondì, A. Cingolani, M. Rivano Capparuccia, G. Iaiani, A. Latini, G. Onnelli, M.M. Plazzi, G. De Girolamo, A. Vergori (Roma); M. Cecchetto, F. Viviani (Rovigo); G. Madeddu, A. De Vito (Sassari); B. Rossetti, F. Montagnani (Siena); A. Franco, R. Fontana Del Vecchio (Siracusa); C. Di Giuli (Terni); P. Caramello, G. Di Perri, S. Bonora, G.C. Orofino, M. Sciandra (Torino); A. Londero (Udine); V. Manfrin, G. Battagin (Vicenza); G. Starnini, A. Ialungo (Viterbo).

***Financial support.*** The ICONA Foundation is supported by unrestricted grants from Gilead Sciences, Janssen, MSD, and ViiV Healthcare. The funders had no role in the study design, data collection, analysis, decision to publish, or preparation of the manuscript.



Table 1. Questionnaires according to different groups of participant to web survey. A) Physician; B) PLWHA; C) PHUS

<b>A) Physicians</b>	<b>N of respondent (%)</b>
Do you know the concept U=U? Yes	83 (92.2)
How do you think U=U be accurate? Completely Enough Not accurate	66 (79.5) 13 (15.7) 4 (4.8)
How much time during the visit do you spend to transact the concept of U=U? Very Enough Little	12 (16.9) 48 (67.6) 11 (15.5)
Do you think the patients have perceived the concept of U=U? Very Enough little	8 (11.3) 35 (49.3) 28 (39.4)
Has the center prepared brochures, posters or other information modes to explain the concept of U=U? No, just medical counselling Yes, informative brochures, posters, etc...	55 (61.1) 35 (38.9)
How frequently have the determination of plasma HIV-RNA in your center been performed? Every 6 months Every 3-4 months	46 (63.0) 27 (37.0)
The knowledge of U=U has changed the frequency of HIV-RNA determination in your center? Yes No	13 (18.3) 58 (81.7)
Who do you focus on most in communicating the U=U concept during the visit? Patients with stable relationship with HIV-pos partner Patients with stable relationship with HIV-neg partner On any patient, without distinction.	11 (15.5) 3 (4.2) 57 (80.3)

<b>B) PLWHA</b>	<b>N of respondent (%)</b>
Have you ever heard of U=U? Yes	296 (74.5)
How do you think U=U be accurate? Completely Enough Not accurate	238 (80.4) 54 (18.2) 4 (1.3)
How U=U changes your sexual/affective activity? Very Enough Little Not at all	127 (42.9) 85 (28.7) 50 (16.9) 34 (11.5)
How U=U changes your feeling about being stigmatized for having HIV? Very	101 (34.1)



Enough	67 (22.6)
Little	78 (26.3)
Not at all	50 (16.9)
With your ID physician do you talk about the possibility of having not protected sexual activity?	
No, he/she says I have to use condom	158 (39.8)
Yes, but he/she says I should inform always sexual partner	108 (27.2)
Yes, he/she says I can have unprotected sex if I'm undetectable	131 (33.0)
Which is the most correct statement regarding your physician and U=U?	
He/she informed me about U=U	150 (50.7)
We never spoke about U=U during visits	63 (21.3)
I asked information to him/her about U=U	83 (28.0)
Where did you get the the information about the message U=U?	
ID Physician	140 (47.3)
Web	145 (49.0)
Community	85 (28.7)
Friends	23 (7.8)

<b>C) PHUS</b>	<b>N of respondent (%)</b>
Have you ever heard of U=U?	
Yes	297 (46.8)
How do you think U=U be accurate?	
Completely	200 (67.3)
Enough	90 (30.3)
Little	5 (1.7)
Not accurate	2 (0.7)
How much U=U changes your sexual/affective activity towards a possible HIV+ partner?	
TotallyEnough	88 (29.4)
Little	87 (29.1)
Not at all	66 (22.1)
	58 (19.4)

Table 2. Sociodemographic characteristics of 1121 participants to web survey, splitted by groups of respondent.

	<b>PLWHA (n= 397)</b>	<b>PHUS (n= 634)</b>	<b>ID physician (n=90)</b>
Age, years, n(%)			
<40	122 (30.7)	461 (72.7)	49 (54.4)
40-50	124 (31.2)	110 (17.3)	18 (20.0)
>50	151 (38.0)	63 (9.9)	23 (25.6)
Gender, male, n(%)	324 (81.6)	431 (68)	37 (41.1)
Nationality, Italian, n (%)	375 (94.5)	610 (96.4)	90 (100)
Italian geographic zone			
North	235 (59.2)	415 (67.5)	46 (51.1)
South/island	45 (11.3)	115 (18.2)	38 (42.2)
Center	117 (29.5)	102 (116.1)	6 (6.7)
Education level, University, n (%)	157 (39.6)	392 (61.8)	90 (100)
Years with HIV infection, n (%)		-	-
<5	112 (28.2)		
5-10	98 (24.7)		
>10	187 (47.1)		
Years on ARVs, n (%)		-	-
<5	125 (31.5)		
5-10	113 (28.5)		
>10	159 (40)		
Plasma HIV-RNA undetectable, yes, n(%)	372 (95.4)	-	-
N of sexual partners in the last year, median (IQR)	2 (1-10)	2 (1-10)	-
Sexual orientation, n (%)			-
Heterosexual	131 (33)	224 (35.3)	
BMSM	41 (10.3)	42 (6.6)	
GMSM	225 (56.7)	368 (58)	
Stable sexual partner, n (%)			
Yes, HIV-pos	53 (13.3)	40 (6.3)	-
Yes, HIV-neg	154 (38.8)	272 (42.9)	
Number of PLWHA in care, n(%)			
<100	-	-	36 (49.3)
100-400			15 (20.6)
>400			22 (30.1)
Years of management of PLWHA, n(%)			
<10			39 (53.4)
10-20			15 (20.6)
>20			19 (26)
Last HIV test, n(%)			
<6 months			242 (38.2)
6-12 months			95 (15)
>12 months			176 (27.8)
Never done			121(121)

Table 3. Factors associated with awareness among the three different groups after fitting a logistic regression

<b>A) PLWH</b>	<b>OR</b>	<b>95%CI</b>		<b>p</b>	<b>AOR*</b>	<b>95%CI</b>		<b>p</b>
Male (vs. Female)	2.49	1.46	1.46	0.001	2.42	1.30	4.50	0.005
Age, years								
<40	1.00				1.00			
40-50	0.51	0.28	0.28	0.029	0.46	0.24	0.89	0.020
>50	0.51	0.28	0.28	0.023	0.62	0.31	1.26	0.189
Time form first ART start								
<5 years	1.00				1.00			
5-10 years	2.17	1.12	1.12	0.021	2.62	1.30	5.28	0.007
>10 years	0.74	0.44	0.44	0.250	1.03	0.56	1.92	0.920
Partner								
No stable relationship	1.00				1.00			
Stable relationship HIV- partner	0.86	0.52	0.52	0.546	0.71	0.39	1.30	0.265
Stable relationship HIV+ partner	0.64	0.33	0.33	0.188	0.72	0.34	1.52	0.386
Number of partner during last year								
0 partner	1.00				1.00			
1 partner	1.29	0.61	0.61	0.506	1.17	0.49	2.80	0.730
2-9 partners	1.09	0.51	0.51	0.818	0.72	0.30	1.70	0.452
>=10 partners	2.50	1.10	1.10	0.029	1.22	0.48	3.12	0.681
Italian zone								
Central	1.00				1.00			
Northern	1.30	0.79	0.79	0.295	1.22	0.72	2.06	0.466
Southern	1.97	0.83	0.83	0.121	2.57	1.03	6.39	0.043
<i>*Adjusted for all the factors showed in table</i>								
<b>B) ID physicians</b>	<b>OR</b>	<b>95%CI</b>		<b>p</b>				
Male (vs. Female)	0.25	0.05	1.37	0.111				
Age								
<40								
40-50	1.51	0.16	14.50	0.720				
>50	0.93	0.16	5.50	0.939				
Managment of HIV patients								
No	1.00							
Yes	14.79	2.57	85.14	0.003				
Number of HIV patients in the center								
<500	1.00							
500-1000	0.55	0.09	3.20	0.506				
>1000	7.80	0.77	79.46	0.083				
Italian zone								
Central	1.00							
Northern	0.22	0.02	1.98	0.178				
Southern	0.14	0.01	2.52	0.180				
<i>*Adjusted for all the factors showed in table</i>								
<b>C) PHUS</b>	<b>OR</b>	<b>95%CI</b>		<b>p</b>	<b>AOR*</b>	<b>95%CI</b>		<b>p</b>
Gender								
Female	1.00				1.00			
Male	1.33	0.94	1.860	0.103	0.75	0.43	1.31	0.313

Female-to-male TG	0.68	0.06	7.674	0.759	3.67	0.26	50.95	0.333
Age. years								
<40	1.00				1.00			
40-50	4.05	2.56	6.41	<0.001	4.51	2.69	7.57	<0.001
>50	1.78	1.05	3.02	0.033	2.92	1.55	5.50	0.001
Education								
University	1.00				1.00			
Secondary/College	0.56	0.40	0.78	<0.001	0.49	0.33	0.72	<0.001
Last HIV test								
<6 months	1.00				1.00			
6months-1 year	0.78	0.48	1.26	0.313	0.68	0.40	1.16	0.156
>1 year	0.51	0.35	0.76	0.001	0.37	0.22	0.60	<0.001
Never done	0.13	0.07	0.22	<0.001	0.15	0.08	0.29	<0.001
Sexual orientation								
Heterosexual	1.00				1.00			
Bisexual	0.93	0.47	1.84	0.842	1.32	0.57	3.04	0.518
Homosexual	1.65	1.18	2.32	0.003	1.40	0.78	2.52	0.253
Partner								
No stable relationship	1.00				1.00			
Stable relationship HIV- partner	1.19	0.86	1.65	0.293	1.27	0.81	2.00	0.289
Stable relationship HIV+ partner	2.70	1.34	5.42	0.005	1.87	0.85	4.12	0.119
Number of partner during last year								
0 partner	1.00				1.00			
1 partner	2.53	1.25	5.10	0.010	1.52	0.66	3.52	0.323
2-9 partners	2.14	1.04	4.39	0.038	1.33	0.58	3.07	0.502
10-49 partners	3.48	1.67	7.27	0.001	1.44	0.60	3.45	0.410
50+ partners	10.00	3.71	26.93	0.000	3.52	1.14	10.87	0.029
Italian zone								
Central	1.00				1.00			
Northern	1.00	0.66	1.52	0.989	1.08	0.67	1.75	0.757
Southern	0.49	0.28	0.85	0.011	0.60	0.31	1.15	0.121

*\*Adjusted for all the factors showed in table*

Table 4 Factors associated with perceiving high accuracy among three groups after fitting a logistic regression

<b>A) PLWH</b>	<b>OR</b>	<b>95CI%</b>	<b>p</b>	<b>AOR*</b>	<b>95%CI</b>	<b>p</b>		
Male (vs.Female)	1.10	0.50	2.45	0.811	0.79	0.32	1.92	0.599
Age. years								
<40	1.00				1.00			
40-50	1.87	0.87	4.02	0.110	2.10	0.93	4.74	0.075
>50	1.08	0.56	2.07	0.825	1.18	0.51	2.70	0.699
Time form first ART start								
<5 years	1.00				1.00			
5-10 years	1.07	0.52	2.2	0.860	0.90	0.41	2.00	0.796
>10 years	0.94	0.47	1.89	0.861	1.00	0.41	2.42	0.992
Partner								
No stable relationship	1.00				1.00			
Stable relationship HIV- partner	1.02	0.56	1.88	0.941	1.36	0.64	2.87	0.427
Stable relationship HIV+ partner	1.60	0.57	4.47	0.367	2.34	0.74	7.38	0.146
Number of partner during last year								
0 partner	1.00							
1 partner	0.66	0.23	1.93	0.449	0.58	0.18	1.93	0.376
2-9 partners	0.63	0.21	1.89	0.406	0.72	0.22	2.38	0.594
>10 partners	1.46	0.46	4.62	0.521	1.73	0.49	6.10	0.396
Italian Zone								
Central	1.00				1.00			
Northern	1.06	0.54	2.06	0.868	1.10	0.55	2.20	0.785
Southern	0.75	0.30	1.91	0.552	0.87	0.31	2.38	0.781
Info about U=U by Association/Community	1.70	0.85	3.39	0.135	2.15	0.97	4.75	0.059
Info about U=U @Hospital	1.47	0.82	2.64	0.195	2.09	1.03	4.25	0.042
Info about U=U on Internet	1.13	0.64	2.01	0.679	1.57	0.78	3.18	0.208

*\*Adjusted for all the factors showed in table*

<b>B) ID physicians</b>	<b>OR</b>	<b>95CI%</b>	<b>p</b>	
Male (vs. F)	2.39	0.71	8.13	0.161
Age				
<40	1.00			
40-50	0.18	0.04	0.75	0.018
>50	0.20	0.05	0.77	0.019
Managment of HIV patients				
No	1.00			
Yes	1.36	0.32	5.68	0.676
Number of HIV patients in the center				
<500	1.00			
500-1000	.	.	.	.
>1000	0.48	0.12	1.89	0.293
Italian zone				
Central	1.00			
Northern	0.19	0.05	0.73	0.016
Southern	0.35	0.03	4.25	0.412

*\*Adjusted for all the factors showed in table*

<b>C) PHUS</b>	<b>OR</b>	<b>95CI%</b>	<b>p</b>	<b>AOR*</b>	<b>95CI%</b>	<b>p</b>		
Gender								
Female	1.00			1.00				
Male	0.76	0.44	1.32	0.333	0.54	0.21	1.39	0.200
Age, years								
<40	1.00			1.00				
40-50	1.10	0.63	1.93	0.740	1.28	0.66	2.48	0.474
>50	1.05	0.48	2.28	0.911	1.29	0.46	3.60	0.631
Education								
University	1.00			1.00				
Secondary/College	0.57	0.34	0.96	0.034	0.54	0.29	0.99	0.045
Last HIV test								
<6 months	1.00			1.00				
6months-1 year	0.53	0.27	1.04	0.063	0.50	0.23	1.09	0.082
>1 year	0.64	0.36	1.16	0.145	0.57	0.26	1.26	0.162
Never done	0.44	0.17	1.15	0.093	0.38	0.12	1.23	0.106
Sexual Orientation								
Heterosexual	1.00			1.00				
BMSM	0.81	0.27	2.43	0.701	0.77	0.19	3.08	0.709
GMSM	1.01	0.59	1.73	0.961	0.81	0.31	2.09	0.662
Partner								
No stable relationship	1.00			1.00				
Stable relationship HIV- partner	0.64	0.39	1.06	0.086	0.59	0.30	1.16	0.128
Stable relationship HIV+ partner	3.43	0.98	12.01	0.054	3.83	1.00	14.67	0.050
Number of partner during last year								
0 partner	1.00			1.00				
1 partner	0.63	0.16	2.47	0.508	0.55	0.11	2.69	0.460
2-9 partners	0.52	0.13	2.10	0.362	0.54	0.10	2.79	0.463
10-49 partners	0.81	0.20	3.29	0.768	0.50	0.10	2.44	0.391
50+ partners	1.67	0.33	8.43	0.537	1.09	0.17	7.04	0.926
Italian zone								
Central	1.00			1.00				
Northern	1.08	0.58	2.02	0.799	1.26	0.61	2.60	0.528
Southern	0.77	0.32	1.87	0.563	1.36	0.47	3.93	0.567
Info about U=U by								
Association/Community	2.73	1.55	4.81	0.001	2.80	1.50	5.23	0.001
Info about U=U @Hospital	1.84	1.05	3.20	0.033	1.84	0.95	3.59	0.072
Info about U=U on Internet	0.70	0.43	1.14	0.155	1.04	0.57	1.89	0.897

*\*Adjusted for all the factors showed in table*

Figure 1. Intracenter concordance between accuracy of perception of physicians and PLWH (within the 4 centers with the highest number of Physician/PLWH respondent).

Supplemental material.

Table 1s. Comparison between PLWH who respond the survey and patients enrolled in the Icona cohort followed in the same centers and period.

	<b>Icona Cohort N=4,564</b>		<b>Survey Respondant N=397</b>		<b>p-value</b>
Gender, n(%)					0.149
Male	3667	80.35	324	81.6	
Female	897	19.6	73	18.39	
TG	38	0.83	0	0	
Italian zone, n(%)					0.116
Northern Italy	2.456	53.81	235	59.19	
Central Italy	1.504	32.95	235	29.47	
Souther Italy	604	13.23	45	11.34	
Italian-Native, n(%)	3833	83.9	375	94.5	<0.001
Age, years, median (IQR)	48	39-56	47	37-55	0.039
Age strata, years, n(%)					0.202
<40	1.233	27.02	122	30.73	
40-50	1.440	31.55	126	31.74	
>50	1.891	41.43	149	37.53	
Mode of HIV Transmission, n(%)					<0.001
Hetero	1.725	37.8	87	21.91	
IDU	427	9.36	31	7.81	
GBMSM	2.136	46.8	246	61.96	
Other/Unknown	276	6.05	33	8.31	
Education level, n(%)					<0.001
Elementary	210	4.6	2	0.5	
Middle school	922	20.2	57	14.36	
High school	1.439	31.53	181	45.59	
University	605	13.26	157	39.55	
Unknown	1.388	30.41	0	0	
Years from HV diagnosis, n(%)					<0.001
<5 years	1.875	41.08	112	28.21	
5-10 years	1.258	27.56	98	24.69	
>10 years	1.431	31.35	187	47.1	
Years from first ART start, n(%)					<0.001
< 5 years	1.981	43.4	125	31.49	
5-10 years	1.448	31.73	113	28.46	
>10 years	909	19.92	159	40.05	
ART-naive	226	4.95	0	0	
Current HIV-RNA, <50 copies/mL, n(%)	4.230	92.7	372	93.7	<0.001



## References

- 1 Attia S, Egger M, Muller M, Zwahlen M, Low N. (2009) Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and metaanalysis. *AIDS*. 23(11):1397–404. DOI: 10.1097/QAD.0b013e32832b7
- 2 Das M, Chu PL, Santos G-M, Scheer S, Vittinghoff E, McFarland W, Colfax GN.(2010) Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS One* 5(6):e11068. doi: 10.1371/journal.pone.0011068.
- 3 Eshleman SH, Hudelson SE, Redd AD, Swanstrom R, Ou SS, Zhang XC, Ping LH, Piwowar-Manning E, Porcella SF, Sievers MF, Martens CA, Bruno D, Dukhovlinova E, McCauley M, Gamble T, Fogel JM, Sabin D, Quinn TC, Gunde L, ....., Cohen MS (2017) Treatment as prevention: characterization of partner infections in the HIV prevention trials network 052 trial. *J Acquir Immune Defic Syndr* 74 (1):112–6. doi: 10.1097/QAI.0000000000001158.
- 4 Rodger AJ, Cambiano V, Bruun T, Vernazza P, Collins S, Van Lunzen J, Corbelli GM, Estrada V, Geretti AM, Beloukas A, Asboe D, Viciano P, Gutiérrez F, Clotet B, Pradier C, Gerstoft J, Weber R, Westling K, Wandeler G, ....., Lundgren J; PARTNER Study Group (2016). Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA*. 316(2):171–81. doi: 10.1016/S0140-6736(16)30418-0
- 5 Bavinton BR, Jin F, Prestage G, Zablotska I, Koelsch KK, Phanuphak N, Grinsztein B, Cooper DA, Fairley C, Kelleher A, Triffitt K, Grulich AE (2014). The Opposites Attract Study of viral load, HIV treatment and HIV transmission in serodiscordant homosexual

male couples: design and methods. *BMC Public Health*. 2014;14(1):917. doi: 10.1186/1471-2458-14-917.

6 Grulich AE, Bavinton BR, Jin F, Prestage G, Zablotska I, Koelsch K. (2015) HIV transmission in male serodiscordant couples in Australia, Thailand and Brazil. Seattle, Washington: 22nd Conference on Retroviruses and Opportunistic Infections.

7 Card KG, Armstrong HL, Lachowsky NJ, Cui Z, Sereda P, Carter A, Montaner JSG, Hogg RS, Roth EA, Moore DM. (2018) Belief in treatment as prevention and its relationship to HIV status and behavioral risk. *J Acquir Immune Defic Syndr*. 2018; 77(1):8–16 doi: 10.1097/QAI.0000000000001557.

8 Carter A, Lachowsky N, Rich A, Forrest JI, Sereda P, Cui Z, Roth E, Kaida A, Moore D, Montaner G, Hogg RS . (2015) Gay and bisexual men’s awareness and knowledge of treatment as prevention: findings from the Momentum Health Study in Vancouver, Canada. *J Int AIDS Soc*. 2015;18(1):20039. DOI: 10.7448/IAS.18.1.20039

9 Holt M, Lea T, Schmidt HM, Murphy D, Rosengarten M, Crawford D, Ellard J, Kolstee J, de Wit J (2016). Increasing belief in the effectiveness of HIV treatment as prevention: results of repeated, national surveys of Australian gay and bisexual men, 2013-15. *AIDS Behav*. 20(7):1564–71. doi: 10.1007/s10461-016-1306-0.

10 “We must listen to science, not stigma. People on effective HIV treatment cannot pass on the virus “ [press release]. Terrence Higgins Trust, June 29, 2017.

11 d'Arminio Monforte A, Lepri AC, Rezza G, Pezzotti P, Antinori A, Phillips AN, Angarano G, Colangeli V, De Luca A, Ippolito G, Caggese L, Soscia F, Filice G, Gritti F, Narciso P, Tirelli U, Moroni M. (2000). Insights into the reasons for discontinuation of the first highly active antiretroviral therapy (HAART) regimen in a cohort of antiretroviral naive patients. *AIDS* 14:499-507. doi: 10.1097/00002030-200003310-00005.

- 12     Huntingdon B, de Wit J, Duracinsky M, and Juraskova I. (2020) Belief, Covariates, and Impact of the “Undetectable = Untransmittable” Message Among People Living with HIV in Australia. *AIDS Patients Care and STDs*, 34 (5):205-212. doi: 10.1089/apc.2019.0300.
- 13     Carneiro P, Westmoreland DA, Patel VV, Grov C. (2020) Awareness and Acceptability of Undetectable = Untransmittable Among a U.S. National Sample of HIV-Negative Sexual and Gender Minorities. *AIDS Behav*. Sep 8. doi: 10.1007/s10461-020-02990-3. Online ahead of print.
- 14     Rendina HJ and Parsons JT (2018) Factors associated with perceived accuracy of the Undetectable = Untransmittable slogan among men who have sex with men: Implications for messaging scale-up and implementation *Journal of the International AIDS Society*, 21:e25055. doi: 10.1002/jia2.25055.
- 15     Torres TS, Cox J, Marins LM, et al. A call to improve understanding of Undetectable equals Untransmittable (U = U) in Brazil: a web-based survey. *J Int AIDS Soc*. 2020;23(11):e25630. doi:10.1002/jia2.25630
- 16     Bor J, Fischer C, Modi M, et al · Changing Knowledge and Attitudes Towards HIV Treatment-as-Prevention and “Undetectable = Untransmittable”: A Systematic Review . *AIDS Behav* 2021; 25(12):4209-4224.