Received: 25 April 2023 | Accepted: 30 October 2023

DOI: 10.1111/hiv.13580

ORIGINAL ARTICLE

HIV pre-exposure prophylaxis services, provision, and delivery in the European treatment network of HIV, hepatitis and global emerging infectious diseases (NEAT ID)

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Abstract

Objectives: We conducted a survey to evaluate HIV pre-exposure prophylaxis (PrEP) practices in a European clinical research network on HIV, hepatitis, and global infectious diseases (NEAT ID).

Methods: An online survey comprising 22 questions was sent via a secure electronic tool to the investigating physician of each of the 342 NEAT ID study centres across 15 European countries in November 2020.

Results: In total, 50 sites from 12 countries responded (15% response rate). Most sites were in Western Europe, two were in Poland, and one was in Hungary. Of the responding sites, 45 provided PrEP services for a total of 27 416 PrEP users, with 1361 new PrEP initiators each month. These centres supplied PrEP for men who have sex with men (100%), people who inject drugs (84%), sex workers (84%), women (62%), and transgender women (31%). PrEP persistence after 1 year was >90%, 75%–90%, and 40%–75% in 17, 24, and 4 centres, respectively. In total, 32/45 (71%) centres reported strong community-based organization commitment at their site, and 15/45 (33%) centres developed task-shifting processes to deliver PrEP through nurses (11/15), pharmacists (5/15), and key-population peers (2/15). The biggest barriers to implementation of PrEP were low awareness of and knowledge about PrEP (47%), unwillingness to disclose sexual identity or at-risk behaviour (36%), and lack of administrative support (29%). Of the 45 centres, 32 (71%) have already been involved in PrEP research and 43 (96%) were interested in participating in such studies.

[†] Members are listed in the Appendix.

Conclusions: The few NEAT ID centres that responded to the survey showed disparities in PrEP deployment and practices despite a common interest in participating in research in this field.

KEYWORDS
Europe, HIV, network, PrEP, provision, uptake

INTRODUCTION

Over the last 10 years, pre-exposure prophylaxis (PrEP) for HIV has become the most important breakthrough in HIV-prevention strategies. Large PrEP roll-out, as part of a combination HIV-prevention approach, has been shown to be effective in significantly reducing the number of new HIV infections at the population level [1]. PrEP integration into comprehensive HIV-prevention programmes became a major priority in the effort to reach the United Nations sustainable development goal of ending the HIV/AIDS epidemic by 2030. Since the release of the ANRS IPERGAY and PROUD PrEP clinical trial results in 2015, PrEP has been gradually rolled out in the World Health Organization (WHO) European region [2, 3]. In 2021, the European Centre for Disease Prevention and Control (ECDC) estimated that about 130 000 individuals received at least one PrEP prescription in the previous year in Europe and Central Asia [4]. Despite this rising number of PrEP users, it was estimated that 500 000 men who have sex with men (MSM) could not access PrEP in the European Union in 2019 [5]. In addition, heterosexual men and women, people who inject drugs, trans people, and sex workers, who accounted for about 80% of new HIV diagnoses in the WHO European region [6], face restricted access to PrEP programmes in many countries. Therefore, much effort is still needed to fill the PrEP gap in Europe. In 2022, of the 55 WHO European region countries, 38 (69%) had implemented PrEP through their healthcare system, 30 (55%) had developed PrEP guidelines, and 23 (42%) were reimbursing PrEP [4]. PrEP barriers in Europe are multidimensional and occur at all stages of the PrEP care continuum [7]. These hurdles can be partially overcome with social, economic, and political interventions, but a firm commitment from European countries to PrEP research is also needed. The European treatment network of HIV, hepatitis, and global infectious diseases (NEAT ID) is a private nonprofit foundation that promotes research and education projects in HIV, hepatitis, and global infectious diseases. The foundation, through its network, has successfully coordinated and conducted major clinical trials in HIV/AIDS and associated infectious diseases in Europe. With 342 centres in 15 countries, NEAT ID can provide a snapshot of PrEP usage in Europe and may be a promising research platform to accelerate the development of transnational research on PrEP use and HIV prevention in Europe. We conducted a survey to evaluate PrEP practices within the NEAT ID and the interest of associated centres in participating in research about PrEP and preventing sexually transmitted infections (STIs).

MATERIALS AND METHODS

We conducted a quantitative, observational, cross-sectional study. We used a web survey to collect on-site information about PrEP services, provision, and delivery to evaluate the feasibility of conducting PrEP studies within the NEAT ID and to evaluate each centre's willingness to participate in research related to PrEP and STI prevention. As no pre-existing, validated questionnaire was available to gather that information from a clinical research perspective, experienced PrEP researchers in the infectious diseases department of the Saint Louis Hospital in Paris designed a first questionnaire draft. The draft questionnaire was subject to thorough discussion, modification, and validation by a committee comprising NEAT ID investigators from various countries involved in the steering committee to ensure the questions would be uniformly understood. The survey comprised 22 questions, including both multiple choice and free-text answers, to derive information on the following areas: PrEP use, provision of PrEP services, user profiles, structure and delivery of services, barriers to PrEP roll-out, and PrEP research experience (Table S1). The survey was written solely in English, as all NEAT ID investigators were assumed to be proficient in English. In November 2020, the online questionnaire was emailed using a secure electronic tool to the investigating physician of each NEAT ID study centre. All the investigators were emailed at least one reminder to fill out the survey, and further reminders were sent to investigators who opened but did not complete the survey. The survey was posted with a 4-week window to complete, but this was extended until 31 October 2021 because of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; COVID-19) pandemic in Europe. A formal analysis of responses was conducted after this extended date. The Research Organization (KC) Ltd carried out the survey

administration, data management, and analysis on behalf of NEAT ID. Data were analysed using Microsoft Access. We used descriptive statistics to present the study results. Categorical variables were presented as frequencies and percentages. The qualitative text from the open questions was used to elaborate on and illustrate aspects of the quantitative results. Countries were grouped into two sub-regions (west and centre) according to the ECDC geographical division of the WHO European region. Individual consent was provided by respondents completing the survey. The study did not require ethical approval because no patient data were used and no biomedical intervention was performed.

RESULTS

The survey was posted to 342 centres involved in NEAT ID across 15 European countries. A total of 50 centres (15%) from 12 countries completed the survey. The response rate varied by country, ranging from 2% in Ireland and Hungary to 22% in Spain (Table 1). Most centres that answered the survey provided PrEP services; five centres (three in Spain, one in Poland, and one in the Netherlands) did not. These five centres did not plan to roll out PrEP services in the 12 months following the survey.

The 45 centres providing PrEP services were spread across 11 European countries: 43 sites were from Western Europe (nine in France, eight in Spain, six in the UK, six in Germany, four in Switzerland, two in Portugal, five in Italy, one in Ireland, and two in Belgium) and two were from central Europe (Hungary and Poland) (Figure 1). Based on the centres' declarations, we estimated that 27 416 PrEP users were followed in these clinical sites (Table 1), with 1361 new PrEP initiators each month. Centres in the UK, France, and Spain represented two-thirds of users and PrEP initiators. Centres provided PrEP for MSM (all sites), for people who inject drugs and sex workers (38/45 sites for each; 84%), for cis-women (28/45 sites; 62%), and for trans-women (14/45 sites; 31%). Nine sites also provided PrEP for other groups, including serodiscordant couples until the partner with HIV reaches an undetectable level, heterosexual people with partners from countries with a high HIV prevalence, and heterosexual men who travel for sex. PrEP was delivered to young individuals, including minors, in 28 (62%) clinical sites. The users' preference regarding the dosing regimen was daily PrEP (15/45 sites; 33%), on-demand PrEP (4/45 sites; 9%), or both (26/45 sites; 58%). The proportion of PrEP users lost to follow-up after 1 year was <10% in 17 centres, ranged from 10% to 25% in 24 centres, and was >25% in four centres.

Of the 45 responder sites, 35 involved community-based organizations in their centres (78%), 24 (53%) reported using new medical technologies such as text messages or mobile health applications to engage and retain individuals in PrEP, and 27 (60%) were involved in communication campaigns to promote PrEP among high-risk individuals. A total of 15 centres (33%) were

TABLE 1 Distribution of centres who provided PrEP services in NEAT ID.

Countries	Number of centres	Response rate by country (%)	Estimated PrEP users in follow-up	Proportion among all PrEP users followed	New monthly PrEP initiators	Proportion among all PrEP initiators (%)
Western Europe	**43**		**27 291**	**99.5**	**1346**	**98.6**
Italy	5	10	645	2	15	1
Ireland	1	2	750	3	41	3
Portugal	2	4	900	3	55	4
Switzerland	4	8	1340	5	56	4
Belgium	2	4	2272	8	76	6
Germany	6	12	2337	9	146	11
Spain	8	22	3800	14	284	21
France	9	18	6147	22	328	24
UK	6	12	9100	33	345	25
Central Europe	**2**		**125**	**0.5**	**15**	**1.4**
Poland	1	4	25	0.1	5	0.4
Hungary	1	2	100	0.4	10	1
Total	**45**	**15**	**27 416**	**100**	**1361**	**100**

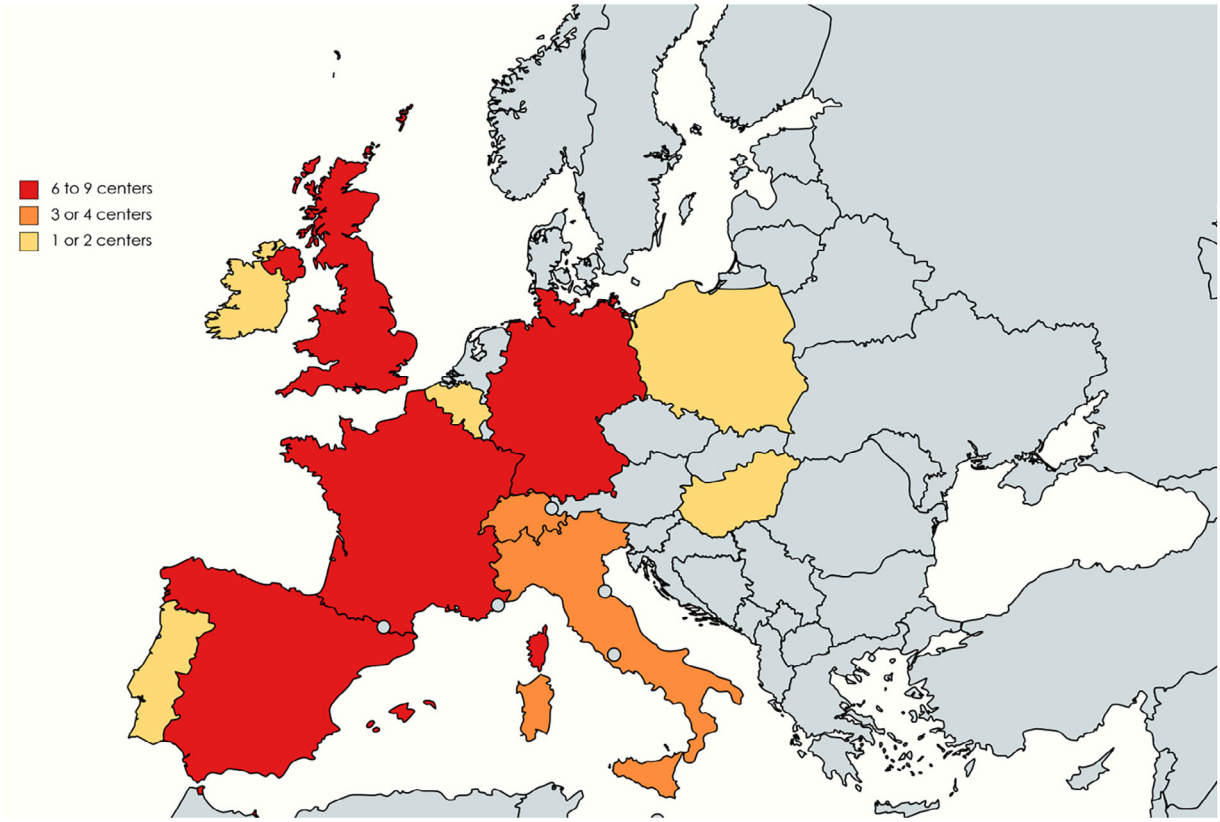

FIGURE 1 Number of responding sites per country.

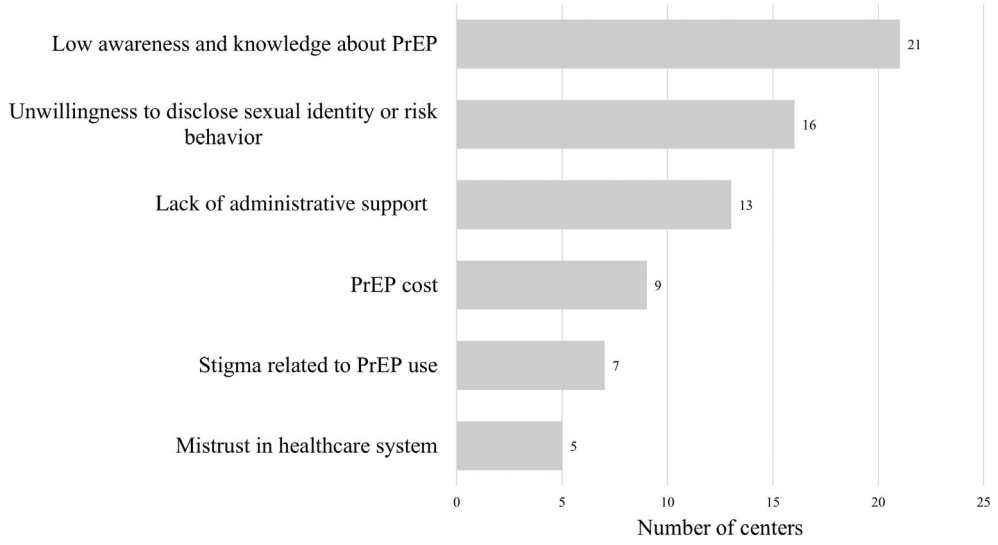

FIGURE 2 Barriers that impacted PrEP roll-out at responding centres. PrEP = pre-exposure prophylaxis.

engaged in task-shifting processes consisting of a non-physician managing PrEP, including nurses (11/15), pharmacists (5/11), key-population peers (2/15), or sexual health advisers (1/15). One site also reported using telemedicine for PrEP delivery. Responder sites also answered questions to identify the barriers that impacted PrEP roll-out at their centres. Results are detailed in Figure 2. The three most significant barriers identified by the sites were a low awareness of and knowledge about PrEP among at-risk individuals (21/45 sites; 47%), the unwillingness of at-risk individuals to disclose their sexual identity or at-risk behaviours (16/45; 36%), and the

lack of commitment by the administration to support PrEP (13/45; 29%). Notably, some sites mentioned that PrEP provision was limited in their countries to specific clinics or that they did not have the human and financial capacity to expand the PrEP services in their centre.

Finally, 32 centres (71%) that responded to the survey have already conducted or participated in clinical studies related to PrEP or STIs, and 43/45 (96%) would agree to participate in such studies within the NEAT ID.

DISCUSSION

This survey aimed to evaluate PrEP practice services, provision, and delivery in the NEAT ID to inform the feasibility of conducting PrEP studies within the network. The results showed that the responding centres were at differing stages of PrEP roll-out. The centres in the UK, France, and Spain accounted for two-thirds of users and PrEP initiators. PrEP provision for groups other than MSM varied greatly, especially for cis- and trans-women. Few centres developed task-shifting processes to deliver PrEP. Individual and structural barriers were the most common hurdles to PrEP implementation, and most sites expressed interest in developing clinical research on PrEP and STIs.

All countries involved in the NEAT ID were represented in the survey, despite a limited response rate (15%). The cumulative number of PrEP users reached about 27 000, which represented 20% of the estimated number of PrEP users in Europe and central Asia, according to the ECDC in 2021 [4]. Our results fully align with a recent survey conducted by the ECDC on PrEP practices in the WHO European region. This study highlighted that PrEP provision was mainly driven by Western European countries, with large variability in terms of availability and reimbursement [4]. The UK, France, and Germany accounted for two-thirds of PrEP users and initiators in Europe and central Asia. As few NEAT centres exist in central Europe, our insights into PrEP practices are limited to the Western European region. Central and Eastern European countries face a high rate of HIV infection, with the largest PrEP gap in Europe [5, 6]. A recent study conducted by the Euroguidelines in Central and Eastern Europe network group showed a slow pace of roll-out in these regions [8]. Of the 22 countries surveyed, 15 (68%) licensed PrEP and 12 (55%) recommended it in their national HIV guidelines. However, despite recent progress, the numbers of PrEP users remain low in the region [8, 9]. Obstacles to rolling out PrEP were mostly structural and related to drug registration and cost or the absence of national guidelines or political commitment. Faster PrEP scaling-up in these countries will be crucial to achieve the United Nations Programme on HIV/AIDS goal for the WHO European region by 2030.

Interestingly, our survey also highlighted that the profiles of PrEP users differed by site. Although all centres delivered PrEP for MSM, only 62% reported following cis-women and 31% reported following trans-women. PrEP implementation efforts mainly focused on MSM in many countries, which results in a low PrEP uptake among heterosexuals at risk of HIV infection. In 2019, the ECDC estimated that less than 10% of PrEP users in Europe were women (including transgender women) or heterosexual men [5]. This was confirmed by a survey conducted by The Women Against Viruses in Europe in 2019, which aimed to explore the availability and implementation of PrEP among women in 34 countries of the WHO European region [10]. The study found that PrEP awareness and acceptability in women remained limited in the region. The major barriers to PrEP uptake were the lack of information and education campaigns targeting women, the absence of specific PrEP guidelines for this population, and the challenges in identifying women at increased risk of contracting HIV. This calls for a holistic approach with multilevel interventions. A strong commitment from all stakeholders is still required to make PrEP a game-changer in the HIV-prevention response among heterosexuals in Europe.

Demedicalization processes are a promising approach to address delivery issues and progress the roll-out of PrEP. Those strategies support task shifting so that PrEP is delivered by non-physicians outside medical settings. As NEAT ID is a hospital-based network, we were unable to evaluate whether PrEP was delivered in other settings, such as primary care, sexual health clinics, or community-based organizations. Nevertheless, our study indicates that one-third of the centres were engaged in task-shifting processes, notably by using registered nurses in PrEP management. This approach still seems limited in Europe. The recent ECDC survey revealed that clinical officers or nurses could prescribe PrEP in only six WHO European countries [4]. Besides this, most countries provide PrEP within infectious diseases clinics, which can constitute a significant barrier for some individuals seeking PrEP. This is another area for improvement to facilitate PrEP access in Europe.

Obstacles to PrEP identified by centres were a mix of individual and structural factors. Low awareness and knowledge among PrEP candidates, as well as the fear of stigma related to sexual identity or behaviour, are well-known factors that hamper PrEP uptake [11]. These data have already been reported in previous PrEP surveys in Europe [4, 8, 9, 12]. This highlights the need for more education about HIV and PrEP and collaboration with community-based organizations to bring more individuals to HIV-prevention services. Compared with previous

European surveys, only a minority of centres mentioned cost as an issue, probably because most sites were in Western European countries, where PrEP is wholly or partially reimbursed. The widespread availability of affordable generic PrEP formulations may also have played a role in addressing cost issues, offering promising prospects for reducing this barrier in many countries. Finally, some centres expressed a need for increased structural support, reflecting the heterogeneous commitment from policymakers towards PrEP development among different European countries.

Almost all responder centres showed a strong interest in participating in clinical studies in PrEP or STIs, and two-thirds have already done so. With nearly 27 000 PrEP users followed in 45 centres across 11 European countries, NEAT ID appears to be a promising research platform to accelerate the development of transnational research on PrEP and STIs in Europe. Potential research areas concern the development and implementation of new PrEP agents and interventions targeting vulnerable and underserved groups to increase PrEP uptake, adherence, and retention. The anticipated arrival of long-acting injectable cabotegravir for HIV prevention offers new research opportunities to strengthen PrEP development in Europe [13]. Recent progress in STI prevention based on doxycycline post-exposure prophylaxis or a vaccinal strategy also opens the door to further studies within the network [14, 15].

Our study has several limitations. First, the survey was launched during the COVID-19 pandemic, which probably impacted the response rate. As a result, the 4-week planned study period had to be extended to 1 year. So, it is unknown whether the questionnaire responses represented usual PrEP practice or adjusted practices during the pandemic. Furthermore, even with the extended duration, only 15% of NEAT ID centres participated in the survey, providing limited insight into PrEP practices within the network. It is likely that centres not providing PrEP chose not to participate in this survey and that PrEP is effectively delivered at few network sites. Second, there was large variability in responses across countries, making it difficult to report a snapshot of, and compare, PrEP practices by country. Estimates of the number of PrEP users and those lost to follow-up by centre may be subject to response bias. Third, the results do not comprehensively depict PrEP practices in Europe. As NEAT ID is a hospital-based network, the study reflects hospital-specific PrEP usage and constraints. Finally, we used mainly pre-defined answers for most survey questions, which limited further exploration of the meaning of the responses. Some linguistic barriers may also be considered as the survey was written only in English.

In conclusion, our study showed disparities in PrEP deployment and practices among the few NEAT ID sites who answered the survey but a common interest in participating in research in this field.

AUTHOR CONTRIBUTIONS

GL and JMM designed the survey. The NEAT ID steering committee validated the survey. AD, CB, and HH sent the survey, collected the data, and wrote the statistical report. GL, JMM, AD, CB, and HH analysed the data. GL wrote the first draft of the manuscript. All authors critically reviewed and approved the manuscript. The results of the study were presented as a poster communication at the HIV Glasgow Congress 2022, 23–26 October 2022, Glasgow, UK [poster P016].

ACKNOWLEDGEMENTS

The authors thank all the centres involved in NEAT ID who took the time to respond to the survey. We are grateful to Polly Parks, the NEAT ID Foundation executive assistant, who helped to coordinate this survey.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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How to cite this article: Liegeon G, Duffy A, Brooks C, et al. HIV pre-exposure prophylaxis services, provision, and delivery in the European treatment network of HIV, hepatitis and global emerging infectious diseases (NEAT ID). *HIV Med*. 2023;1-8. doi:10.1111/hiv.13580

APPENDIX

TABLE S1 Survey questionnaires.

Q1	**Are you providing PrEP services?**
Q2	If not, are you planning to provide PrEP within the next 12 months?
Q3	What is (are) the profile(s) of PrEP user(s) at your center? Possible answers: *[MSM], [TGW], [PWID], [SEX WORKERS], [WOMEN], [Others]*
Q4	If others, please tell us about these other types of users:
Q5	How many PrEP users are currently under follow-up at your center?
Q6	How many individuals initiate PrEP each month?
Q7	Are you providing PrEP for young individuals including minors (< 20 years)?
Q8	If yes, could you estimate the number?
Q9	What is the users' preference regarding PrEP regimen at your center?
Q10	In your PrEP program, what is the percentage of PrEP users who are lost to follow-up one year after starting PrEP?
Q11	Is there a strong commitment of community-based organisation at your center?
Q12	Are you involved in PrEP de-medicalisation strategies (by giving the opportunity to non-physicians to deliver PrEP)?
Q13	If yes, please let us know which personnel are involved in the delivery: *[Key population led health service model], [Pharmacist], [Nurses], [Others?]*
Q14	If others, please tell us about these personnel types:
Q15	Do you use new medical technologies (text message, mobile health application...) to engage and retain individuals at risk of HIV infection in PrEP?
Q16	Are you involved in communication campaigns to promote PrEP among high-risk individuals?
Q17	At your center, what is the situation concerning PrEP training?
Q18	What are the biggest barriers impacting PrEP roll-out at your center? Possible answers *[Low awareness and knowledge about PrEP among at-risk individuals], [Unwillingness of individuals at-risk to disclose sexual identity or at-risk behavior], [Stigma related to PrEP use], [Mistrust in health care system], [Lack of commitment of administration], [PrEP cost], [Others?]*
Q20	What are the biggest barriers impacting PrEP roll-out at your center?
Q21	If others, please tell us about the biggest barriers impacting PrEP roll-out at your center:
Q22	Have you already conducted or participated to clinical studies related to PrEP at your center?
Q23	Would you be interested to participate to clinical studies on PrEP within the network?
Q24	Would you be interested to participate to clinical studies on STIs within the network?

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