Aus der Klinik für Dermatologie, Venerologie und Allergologie der

Medizinischen Fakultät Charité – Universitätsmedizin Berlin

DISSERTATION

HIV Pre-exposure Prophylaxis in Germany: Barriers and Strategies to Improve Uptake

HIV-Präexpositionsprophylaxe in Deutschland: Barrieren und Strategien zur Verbesserung der Implementierung

zur Erlangung des akademischen Grades

Doctor medicinae (Dr. med.)

vorgelegt der Medizinischen Fakultät

Charité – Universitätsmedizin Berlin

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Datum der Promotion: 29 November 2024

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List of Abbreviations

AIDS	-	Acquired immunodeficiency syndrome
ART	-	Antiretroviral therapy
BIPOC	-	Black, Indigenous and other People of Color
CAI	-	Condomless anal sex
CDC	-	Centers for Disease Control and Prevention
DAIG	-	Deutsche AIDS Gesellschaft *(German AIDS Association)*
DSTIG	-	Deutsche STI Gesellschaft *(German STI Association)*
HAART	-	Highly active antriretroviral therapy
HIV	-	Human immunodeficiency virus
HIVSP	-	HIV specialists
nHIVSP	-	Non-HIV specialists
IQR	-	Interquartile range
KBV	-	Kassenärztliche Bundesvereinigung *(National Association of Statutory Health Insurance Physicians)*
LGBTQI+	-	Lesbian, gay, bisexual, transgender, queer, intersex and others
LHO	-	Local health office
MSM	-	Men who have sex with men
NGO	-	Non-governmental organization
SD	-	Standard Deviation
SOP	-	Standard Operation Procedure
STI	-	Sexually transmitted infection
TDF/FTC	-	Emtricitabine / tenofovir disoproxil fumarate (*Tenofovir)*

Abstract

1.1 Abstract (English)

Background

HIV pre-exposure prophylaxis (PrEP) has been shown to be both safe and highly effective in preventing HIV infection in a range of clinical trials and cohort studies. PrEP has also been integrated into many national HIV prevention guidelines, including Germany's since 2018. The German statutory health insurance began coverage for PrEP and all associated costs in September 2019. The aim of our studies was to identify potential barriers to PrEP use, as well as any advisement and/or treatment gaps so as to improve PrEP implementation across Germany.

Methods

All three studies utilized in-house developed questionnaires. The first study was a multicenter, paper-based survey of adult men who have sex with men (MSM) in Berlin with unknown or negative HIV status between October 2017 and April 2018. The second study was an online questionnaire of counsellors and health departments across Germany between October and December 2018. The third study was a paper- and online-based questionnaire of general practitioners, internists, urologists and dermatologists between August and October 2019. For the second and third papers, knowledge and attitude scores were calculated from items from both aspects with scores ranging from zero to 20. Higher scores represented greater knowledge or more positive attitudes.

Results

The first paper indicated that less than half of participants felt well-informed about PrEP (48.2%) and informed themselves most infrequently via doctors (22.7%) and counselling centers (13.9%). A high rate of informal PrEP use was seen, and a fourth of non-PrEP users cited high-risk sexual activity.

The second paper indicated that the knowledge and attitude of the individual counsellors – irrespective of center type - were independent predictive factors for proactive PrEP advisement. Furthermore, the knowledge of PrEP and the attitudes toward PrEP were more positive among counsellors from non-governmental counselling centers compared to counsellors from local health departments.

The third paper showed greater self-assessed knowledge and more positive attitudes towards PrEP among HIV specialists than non-specialists; however, multiple regression analyses suggested the only independent predictive factor for proactive PrEP advisement was the physician knowledge – not their status as HIV specialist or non-specialist.

Conclusions

The findings of our studies illustrate a need for PrEP advisement from knowledgeable sources and simplified PrEP access. Targeted PrEP training in counseling centers and health departments, as well as simplified physician certification programs can reduce barriers to PrEP certification and help improve PrEP implementation in Germany in both rural and urban centers.

1.2 Abstract (Deutsch)

Hintergrund

Die Präexpositionsprophylaxe (PrEP) hat sich in einer Reihe von klinischen Studien und Kohortenstudien als sicher und hochwirksam erwiesen. Seit 2018 ist die PrEP auch in vielen nationalen HIV-Präventionsleitlinien integriert, so auch in Deutschland. Seit September 2019 übernimmt die gesetzliche Krankenversicherung die Kosten für die PrEP und alle damit verbundenen Leistungen. Ziel unserer Arbeit war es, mögliche Barrieren für die PrEP-Nutzung sowie Beratungslücken und Behandlungslücken zu identifizieren, um die PrEP-Implementierung in ganz Deutschland zu verbessern.

Methoden

In allen drei Studien wurden selbst entwickelte Fragebögen verwendet. Die erste Studie war eine multizentrische, papierbasierte Befragung von erwachsenen Männern, die Sex mit Männern haben (MSM), in Berlin mit unbekanntem oder negativem HIV-Status zwischen Oktober 2017 und April 2018. Die zweite Studie war eine Online-Befragung von Beratern und Gesundheitsämtern in Deutschland zwischen Oktober und Dezember 2018. Bei der dritten Studie handelte es sich um eine papier- und onlinebasierte Befragung von Allgemeinmedizinern, Internisten, Urologen und Dermatologen zwischen August und Oktober 2019. Für die zweite und dritte Studie wurden Wissens- und Einstellungsscores aus Items beider Aspekte berechnet, wobei die Scores von 0 bis 20 reichten. Hohe Werte zeigten gute Kenntnisse oder positive Einstellungen an.

Ergebnisse

Die erste Studie ergab, dass sich weniger als die Hälfte der Teilnehmer gut über PrEP informiert fühlten (48,2 %) und sich am seltensten bei Ärzten 22,7 %) und Beratungsstellen (13,9 %) informierten. Von den Nicht-PrEP-Nutzern gaben circa 25 % risikoreiche sexuelle Aktivitäten an, während unter den PrEP-Nutzern eine hohe Rate an informeller PrEP-Nutzung festgestellt wurde.

Die zweite Studie zeigte anhand von multiplen linearen Regressionsmodellen, dass das Wissen und die Einstellung der einzelnen Berater - und nicht die Art der Beratungsstelle, in der sie tätig sind - unabhängige prädiktive Faktoren für die proaktive PrEP-Beratung sind. Darüber hinaus waren das selbst eingeschätzte

Wissen über die PrEP und die Einstellung zur PrEP bei Beratern aus nichtstaatlichen Beratungsstellen positiver als bei Beratern aus lokalen Gesundheitsämtern.
Die dritte Studie zeigte ein größeres selbst eingeschätztes Wissen und eine positivere Einstellung zur PrEP bei HIV-Spezialisten als bei Nicht-Spezialisten. Unsere multiple Regressionsanalyse ergab jedoch, dass der einzige unabhängige prädiktive Faktor für eine proaktive PrEP-Beratung das Wissen der Ärzte war - und nicht ihr Status als HIV-Spezialist oder Nicht-Spezialist.

Schlussfolgerungen

Die Ergebnisse unserer Studien verdeutlichen den Bedarf an PrEP-Beratung durch informierte Personen und einen vereinfachten PrEP-Zugang. Gezielte PrEP-Schulungen in Beratungsstellen und Gesundheitsämtern sowie vereinfachte ärztliche Zertifizierungsprogramme können die Hürden für die PrEP-Zertifizierung verringern und dazu beitragen, die PrEP-Implementierung in Deutschland sowohl in ländlichen als auch in städtischen Zentren zu verbessern.

1. Introduction

In 2012, the United States approved the HIV pre-exposure prophylaxis (PrEP), most commonly prescribed as the combination pill Truvada [Emtricitabine/Tenofovir Disoproxil Fumarate (TDF/FTC)], as a daily or on-demand oral tablet to prevent HIV among those at risk for infection (2). HIV PrEP was further approved by the European Union in 2016 (3).

Studies have shown PrEP to be effective at reducing the risk of infection with HIV by 73% and up to 90% when taken as directed; even higher rates are seen when taken with greater adherence (4). Multiple studies in a variety of metropolitan areas have illustrated a drastic reduction in their HIV infection incidence rate (5-7).

In recent years, rates of new HIV infections within Germany have stagnated to circa 2,000 to 3,000 cases per year (8, 9); however, population groups such as men who have sex with men (MSM) continue to carry a considerable portion of that burden (8). As of 2020, only 1 in 5 Americans who could benefit from taking PrEP are receiving prescriptions for it (10). Europe has seen similar trends, illustrated in the 2019 study using information gleaned from the European MSM Internet Survey which showed roughly 17.4% of MSM in the European Union who would consceivably use chemoprophylaxis had no proper access to it (11). Ensuring patients who could benefit from PrEP are able to receive quality information about PrEP, know how to access PrEP and receive both a prescription and support while taking PrEP is essential to reducing the burden of disease in populations most at risk.

Studies reviewing implementation research have identified a wide range of barriers that prevent access to, delivery of and adherence to PrEP (12). Implementation research is commonly defined “as the study of processes and strategies that move, or integrate, evidence-based effective treatments [in this case PrEP] into routine use, in usual care settings” (13). When attempting to study the implementation of a medication, many perspectives need to be assessed in order to determine which barriers exist and how they may best be addressed.

One study identified four ecological domains that define PrEP implementation barriers: individual (i.e. the patient), relationship (i.e. a patient-service provider), the community and policy (14). Examples of patient-centered barriers include language barriers, a lack of time to visit prescribers; relationship barriers may include a physician’s negative attitude towards PrEP or the “purview paradox” wherein primary care physicians

(PCPs) who often see uninfected, HIV-negative patients are not trained to provide PrEP while HIV specialists trained to provide PrEP rarely see HIV-negative patients (15). Examples of community-centered barriers include homophobia, HIV stigma or racism; and examples of policy barriers include a lack of coverage for PrEP-associated costs by statutory health insurances.

To fully utilize PrEP's potential to curb HIV infections, interventions need to concentrate on multiple PrEP domains; however, most interventions published in the literature focus on largely one, individual level (e.g. policy-level), which make it hard to truly assess causes of poor PrEP implementation (16). Most published studies have reviewed single-level barriers (i.e. provider-level) but made suggestions for other levels (i.e. policy-level) without any supporting data (12, 16). When seeking to assess barriers to implementation, all areas must be considered, as well as the interplay between them.

Interdisciplinary work between counsellors, social services and public health services with physicians who can provide PrEP prescriptions helps ensure patients can continue along the PrEP pipeline from need identification to prescription (12). This type of interprofessional partnership is important to ensure patients can continue along the PrEP care continuum from identification to prescription to care retention (1). By abstaining from interdisciplinary implementation assessments, the PrEP pipeline is not being adequately reviewed, and potential barriers to prescription and use will not be properly evaluated.

Even without published studies reviewing German PrEP implementation, a multitude of associations have pressured the German statutory health system to begin broad coverage of PrEP, including all necessary testing and prescription costs. While this move surely decreases patients' financial burdens, a true review of PrEP's implementation in Germany has not been undertaken.

The objective of the three papers presented in this dissertation was to evaluate the readiness for implementation of PrEP across all ecological domains: patients, counsellors (from both non-governmental and state-run organizations), and physicians. The work presented provides a cross-sectional assessment of participants' attitudes and perceived barriers to PrEP while making recommendations as to how to better the implementation of PrEP, and, therefore, decrease new cases of HIV across Germany.

2. State of Research

At the time of publication of each of these articles, there was limited previous research to assess patient, counsellor or provider opinions and/or experiences regarding PrEP in Germany. A multitude of studies have been performed worldwide(5, 6, 17) ; however, specific studies from the German perspective had not previously been undertaken. Although Tenofovir/Emtricitabine has been approved for the prevention of HIV infection since 2016, there have been no approved guidelines until 2018. Given that the statutory health insurance began coverage for PrEP in 2019, it was prudent to determine if treatment gaps exist or if knowledge gaps among healthcare professionals are inhibiting patient care. The studies sought to evaluate the perspectives among the main players in the PrEP sphere (patients, counsellors and physicians) to identify (1) what potential barriers currently exist and (2) how we might work around them to improve access to all patients who could benefit from PrEP.

3. Methods

All of the studies listed in this synopsis received approval from the Charité – Universitätsmedizin Berlin's ethics board (EA1/162/17; EA1/006/19). Participants' informed consent was collected, either via oral agreement and subsequent questionnaire completion (publication 1), by checking a box on an online consent form (publications two and three), or by submitting their completed questionnaire via fax (publication three) (18-20).

None of the studies required identifiable information (i.e., full or partial name, street address, or birthdate) to complete the questionnaires. In the first paper, anonymity was ensured by local staff who stored completed questionnaires for collection by study staff (18). In the second publication, anonymity was ensured by refraining from collecting respondents' IP-address information (19). The third publication's paper study ensured anonymity of all faxed questionnaires by having an unrelated staff member remove all identifiable fax numbers before submitting it to the research staff for data collection; the online version did not collect IP-address information (20).

3.1 Publication 1: *Knowledge and use of HIV pre-exposure prophylaxis among men who have sex with men in Berlin - A multicentre, cross-sectional survey*

3.1.1 Study design and setting

The study sought to evaluate the patient and/or community perspective, as well as patient-related barriers to PrEP uptake between October 2017 and April 2018; HIV-negative MSM aged 18 years or older were included in this study(18). We designed a questionnaire to explore diverse attitudes towards PrEP, experiences surrounding PrEP and reasons why patients would or would not take PrEP(18). The questionnaire was available in paper form in both English and German.

3.1.2 Data collection and questionnaire design

We designed a two-page questionnaire with multiple-choice questions allowing for single and multi-choice answers (18). An open-ended question about patients' motivation to take PrEP was also included (18). Sociodemographic data regarding participants' age range, place of residence, current financial circumstances, and family immigration status (i.e., whether respondents were first- or second-generation Germans, immigrants themselves or Germans without immigration backgrounds) (18). Additionally, the following aspects were assessed (18):

- Patient awareness of PrEP and their preferred information sources
- Patient interest in using PrEP and any previous experiences using it
- Barriers to begin or continue PrEP use
- Preferences for intake method and regimen
- Anticipated impact of chemoprophylaxis on future condom use
- Attitudes towards PrEP, including potential cost coverage through the German statutory health insurance system
- Sexual behavior and risk of HIV infection (i.e. date of most recent HIV test, STI diagnoses received within the last 12 months, history of condomless anal intercourse)

The questionnaire was given to patients in 11 HIV specialist practices and 4 non-governmental sexual health and STI testing centers in Berlin (18).

3.2 Publication 2: *HIV Pre-Exposure Prophylaxis (PrEP) Counseling in Germany: Knowledge, Attitudes and Practice in Non-governmental and in Public HIV and STI Testing and Counseling Centers*

3.2.1 Study design and setting

The study sought to evaluate community and counsellor-patient relationships as ecological domains (19). We designed an online questionnaire to explore the attitudes

towards PrEP and advising practices with at-risk patient groups (19). A variety of statements regarding participants' opinions about PrEP and their likelihood of prescribing PrEP to specific patients were assessed using a 5-point Likert scale (19). The questionnaire was sent via email to STI testing centers and local health departments across Germany (19).

3.2.2 Data collection and questionnaire design

We designed an online questionnaire with multiple-choice questions allowing for single and multi-choice answers (19). We obtained sociodemographic data regarding participants' gender, age, professional qualifications, work experience counselling on sexual health, counselling frequency of MSM and trans persons, and experiences testing for HIV (19). Additionally, the following aspects were assessed (19):

- Frequency of counseling sessions with guideline-defined at-risk persons
- Counseling practice with patients at increased risk regarding PrEP
- Self-assessed knowledge of and attitudes towards PrEP
- Need for educational information or training materials in order to improve PrEP advisement abilities
- Barriers to PrEP initiation and adherence

The knowledge and attitudes assessments were studied using a five-point Likert scale with ambivalent centers(19). Summative, multi-item scales are considered more reliable than Likert-scaled variables; therefore, we designed aggregate knowledge and attitudes scores that were calculated using five different variables regarding counsellor knowledge or attitude towards PrEP, see **Table 1** (19). The total score values ranged from 0 (low competence or negative attitude) to 20 (high competence, positive attitude) (19). Data was collected between October and December 2018 (19).

Table 1. Dimensions and their operationalization for assessing (A) Knowledge and counselling competence and (B) attitudes towards PrEP (19).

Dimension		**Operationalization and scores**				
Do you agree or disagree with the following statements?		**Strongly disagree**	**Disagree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
(A) Knowledge and counselling competence						
Global Assessment	"I am well-informed about PrEP"	0	1	2	3	4
Indications	"I am able to comprehensively give clients advice on whether it makes sense to take PrEP in their respective case"	0	1	2	3	4
Adverse effects	"I am able to comprehensively give clients advice on the adverse effects of PrEP"	0	1	2	3	4
Modalities of intake	"I am able to comprehensively give clients advice on the possible modalities of intake of PrEP (e.g., continuous vs on-demand)	0	1	2	3	4
Investigations	"I am able to comprehensively give clients advice on the medical investigations necessary during the use of PrEP"	0	1	2	3	4
Knowledge Score		**Summative score with values ranging from 0 to 20**				
(B) Attitudes towards PrEP						
Global Assessment	"I think that PrEP is an important element of HIV prevention strategies"	0	1	2	3	4
Reliability	"I think that PrEP is a reliable method to protect oneself from HIV"	0	1	2	3	4
Adverse effects	"I think that PREP is a method to protect oneself from HIV that has few side effects"	0	1	2	3	4
Availability of better alternatives	"I think that PrEP is unnecessary, because there are better alternatives to protect oneself from HIV"	4	3	2	1	0
Reimbursement of costs	"I think that PrEP should be paid for by the statutory health insurance"	0	1	2	3	4
Attitudes Score		**Summative score with values ranging from 0 to 20**				

3.3 Publication 3: *HIV Pre-exposure Prophylaxis (PrEP): Knowledge, attitudes and counseling practices among physicians in Germany – A cross-sectional survey*

3.3.1 Study design and setting

The study sought to evaluate barriers in the following ecological domains: physician cognition barriers, patient-physician relationships, and physician policy (20). We designed a questionnaire with Likert scales (five-point and 11-point Likert scales),

multiple-choice questions with both singular and multi-answer options, as well as free text questions pertaining to other perceived PrEP barriers and failed PrEP initiations by patients who could not take PrEP due to testing positive for HIV (20). Physicians from the following specialties were invited: internal medicine, general medicine, urology and dermatology. We employed three methods of recruitment for the study (20):

1) Requesting contact details from the National Association of Statutory Health Insurance Physicians (ger. *Kassenärztliche Bundesvereinigung*, KBV) of a random sample of 2,200 office-based, practicing physicians in the aforementioned specialties (20). The physicians received a paper version of the questionnaire followed by an email reminder with a link to the online questionnaire to those who had email addresses (42% of physicians) (20).
2) Utilizing professional associations' online mailing lists to contact physician members with a link to the online version of our questionnaire (20). Members of the German AIDS Association (ger. *Deutsche AIDS Gesellschaft*, DAIG) (*N*=253) and the German STI Association (ger. *Deutsche STI Gesellschaft*, DSTIG) (*N*=330) were contacted and sent reminder emails two weeks later (20).
3) Placing flyers with a QR Code for the online questionnaire at a national STI conference in Berlin in September 2019 (20).

Data was collected between August and October 2019 (20).

3.3.2 Data collection and variables

At the time of study development, no standardized German-language questionnaire for physicians existed to explore a wide range of aspects relating to PrEP (knowledge, attitudes, counselling and prescription practices) (20). We developed a questionnaire specifically for the purposes of this study (see Supplements 5 and 6) utilizing questionnaire development recommendations described by Crawford and by Aschemann-Pilshofer (21, 22).

With the goal of the study to ascertain knowledge and experience differences that could lead to treatment gaps, we needed to know what type of specialty our physicians practiced, where they are located, what their experiences with PrEP and HIV have been, their knowledge of PrEP, their opinions of PrEP, and what barriers they

perceived to be relevant to patients and physicians (20). A single, double-sided paper questionnaire was drafted with the following question topics:

- Physician respondent data (demographic data about physician and their practice setting)
- Experience with HIV, HIV PrEP and MSM
- Knowledge of PrEP, perception of PrEP
- Perceived barriers for patients and physicians
- Experiences with PrEP failures
- Opinions about PrEP
- Preferences for educational training about PrEP

We collected demographic data which included the participants' medical specialties, whether the practice in which they work was designated as an HIV/AIDS specialty practice (according to the German Quality Assurance Agreement on HIV/AIDS), participant age, participant gender, the languages in which they practiced, as well as the practice location (20). The practice location was determined using the first three numbers of the provided zip code in order to determine the German state and which local region the practice is located (20).

Similarly to the previous questionnaire, a tabularly summary of the German and Austrian recommendations for PrEP was provided, detailing the indications for PrEP to HIV-negative MSM and transgender persons (i.e. defining our "at-risk" patient groups) (19, 20). Referring to an average yearly quarter, physicians were asked how many of the defined patients were (a) seen in their practice, (b) advised on PrEP after patient initiative, (c) advised on PrEP after physician initiative, and (d) received a prescription for PrEP after their visit (20).

As in the previous study, the summative knowledge and attitude scores with five items each were employed in this study to provide a more reliable analysis (19, 20).

4. Statistical Methods

All of the questionnaires designed in these studies were designed specifically for these projects in mind; therefore, we had no expected numbers and performed no formal sample size calculations (18-20). The number of responses we aimed to collect were based purely on feasibility (18-20). The first study's aim was to collect between 400 to 600 responses (18). The second study's collection goal was to match all of the NG

counselling center with comparable local health departments (19). The third study targeted a response size of 2,200 physicians (19). All statistical analyses were performed with IBM® SPSS® Statistics Version 25 (sample characteristics and bivariate statistics) and STATA SE version 14.2 (multiple linear or logistic regressions) (18-20).

In accordance with the quality of the data, we performed descriptive statistics to summarize all sample calculations and a variety of statistical tests to estimate any asociations between the pre-selected variables (Independent sample *t*-tests, Mann-Whitney-*U* tests, Pearson's Chi-squared tests and Fisher's exact tests) (18-20). The first study utilized a Bonferroni-adjustment to resolve issues associated with multiple testing (α-level: 0.005) (18). In accordance with the data, we performed univariate logistic regressions, multivariate linear regressions or multivariate logistic regressions to identify predictors for the primary study endpoints (18-20). In our first study, we employed multivariate logistic regressions to determine positive predictive factors of wanting to initiate PrEP or having had previously taken PrEP, the effects of which were quantified using odds ratios and 95% confidence intervals (18). In the second study, we performed a backwards regression analysis to determine positive predictive factors for proactive PrEP advisement with at-risk clients (19). The third study utilized forward and backward regression analyses to determine predictive factors for proactive PrEP advisement with at-risk HIV patients (20). We determined a fixed stopping rule with a cut-off value for p at 0.075 in our first study (following Bursac, Gauss, Williams and Hosmer) and $p < 0.2$ in the second and third studies (18-20). To prevent multi-collinearity of predictive factors or any instability of the regression coefficients, we utlizied variance inflation factor (VIF) statistics with the level of statistical significant set to $p = 0.05$, and all missing cases were subsequently excluded in a listwise fashion (19, 20). The first study wanted to examine these factors across different sexual risk levels, so new variables across four risk levels were created to prevent collinearity of independent variables (18), see ***Table 2***.

Table 2. Definitions of sexual risk groups according to self-reported total of condomless anal intercourse partners and STIs within the past six months (18)

Label for sexual risk behavior	Definitions (referring to the past six months)
"Highest risk (CAI* + STI)"	Reported having had CAI with two or more partners and a diagnosis of any STI
"Higher risk (CAI)"	Reported having had CAI with two or more partners but no STI diagnosis
"Higher risk (STI)"	Reported having had a diagnosis of any STI but not CAI with two or more partners
Low risk (STI)	Did not report having had an STI diagnosis or CAI with two or more partners

CAI, condomless anal intercourse; *STI*, sexually transmitted infections

Using this method, we were able to estimate the indications for beginning chemoprophylaxis by MSM as recommended by the CDC. "Two or more partners" was chosen as a starting point, as participants may report CAI with one sexual partner ("CAI in a monogamous relationship") (18). As CDC guidance does not differentiate between receptive or insertive CAI, we did not make this distinction either (18).

5. Results

5.1 Publication 1

Demographic data

In total, 875 questionnaires were distributed, and 473 were completed and returned (54.1% response rate) (18). Three respondents reported living with HIV and were removed as part of the exclusion criteria (18). The majority of respondents filled out the questionnaire in German (84.9%), completed a university degree (65.3%), had enough or more than enough money to pay for necessities (87.4%) and were born in Germany to German parents (59.8%) (18). Nearly all patients reported living in Berlin (94.0%) (18).

Sexual Health History

Having an HIV-negative status was part of the study's inclusion criteria (18). All patients reported either being HIV negative (86.4%), unsure of their status (11.1%) or declined to state their HIV status (2.6%) (18). The majority of patients (81.1%) reported not receiving a diagnosis of an STI within the last 6 months (18). Roughly two thirds of respondents reported having anal sex (97.3%) with the majority partaking in penetrative anal sex only, most of the time or at least half of the time (66.4%) (18).

68.1% of respondents reported having two or more anal sex partners within the last six months. Of those respondents reporting anal sex encounters, roughly one third (32.1%) did so without using a condom with at least two or more partners; 28.5% reported a lack of condom use with just one anal sex partner within the last 6 months (18).

Table 3. Demographic data and sexual risk behaviors (18)

		Total sample	Type of center	
			Counselling centers[1]	Doctors practices[2]
N		470	221	249
Age				
	Mean (SD)	37.4 (11.9)	32.9 (8.0)	41.4 (13.2)
	Min; Max	18-79	18-59	19-79
Highest degree or level of school *(n, %)*				
	Primary education	0	0	0
	Secondary education up to year 10*	42 (8.9%)	8 (3.6%)	34 (13.7%)
	Secondary education with apprenticeship	23 (4.9%)	5 (2.3%)	18 (7.2%)
	Secondary education up to year 12**	89 (18.9%)	44 (19.9%)	45 (18.1%)
	University degree	307 (65.3%)	160 (72.4%)	147 (59.0%)
	Not stated	9 (1.9%)	4 (1.8%)	5 (2.0%)
Financial Situation *(n, %)*				
	Not always enough money	51 (10.9%)	23 (10.4%)	28 (11.2%)
	Enough money	205 (43.6%)	95 (43.0%)	110 (44.2%)
	More than enough money	206 (43.8%)	99 (44.8%)	107 (43.0%)
	Not stated	8 (1.7%)	4 (1.9%)	4 (1.6%)
Place of residence *(n, %)*				
	Berlin	442 (94.0%)	204 (92.3%)	238 (95.6%)
	Other city in Germany	10 (2.1%)	4 (1.8%)	6 (2.4%)
	Small town / rural area in Germany	4 (0.9%)	3 (1.4%)	1 (0.4%)
	Other country	8 (1.7%)	7 (3.2%)	1 (0.4%)
	Not stated	6 (1.3%)	3 (1.4%)	3 (1.2%)
Family Origins *(n, %)*				
	Participants & both parents born in Germany	281 (59.8%)	112 (50.7%)	169 (67.9%)
	One parent born outside Germany	32 (6.8%)	19 (8.6%)	13 (5.2%)
	Both parents born outside German	38 (8.1%)	25 (11.3%)	13 (5.2%)
	Participant born outside Germany	112 (23.8%)	62 (28.1%)	50 (20.1%)
	Not stated	7 (1.5%)	3 (1.4%)	4 (1.6%)
Current HIV Status *(n, %)*				
	HIV negative	406 (86.4%)	171 (77.4%)	235 (94.4%)
	Not sure	52 (11.1%)	41 (18.6%)	11 (4.4%)
	Not stated	12 (2.6%)	9 (4.1%)	3 (1.2%)
STI diagnosis in the past six months *(n, %)*				
	No	381 (81.1%)	182 (82.8%)	198 (79.5%)
	Yes	82 (17.4%)	24 (15.4%)	48 (19.3%)
	Not stated	7 (1.5%)	4 (1.8%)	3 (1.2%)
Role when having anal sex *(n, %)*				
	No anal sex	21 (4.5%)	2 (0.9%)	19 (7.6%)
	Bottom only	37 (7.9%)	19 (8.6%)	18 (7.2%)
	More bottom than top	91 (19.4%)	48 (21.7%)	43 (17.3%)
	Top and bottom (versatile)	141 (30.0%)	66 (29.9%)	75 (30.1%)
	More top than bottom	99 (21.1%)	47 (21.3%)	52 (20.9%)
	Top only	72 (15.3%)	33 (14.9%)	39 (15.7%)
	Not stated	9 (1.9%)	6 (2.7%)	3 (1.2%)
Number of anal sex partners in the past six months *(n, %)*				
	None	55 (11.7%)	10 (4.5%)	45 (18.1%)
	1	80 (17.0%)	36 (16.3%)	44 (17.7%)
	2 to 5	142 (30.2%)	85 (38.5%)	57 (22.9%)
	6 to 10	79 (16.8%)	38 (17.2%)	41 (16.5%)
	More than 10	99 (21.1%)	45 (20.4%)	54 (21.7%)
	Not stated	15 (3.2%)	7 (3.2%)	8 (3.2%)
Number of anal sex partners without using condoms in the past six months *(n, %)*				
	None	174 (37.0%)	68 (30.8%)	106 (42.6%)
	1	134 (28.5%)	79 (35.7%)	55 (22.1%)
	2 to 5	109 (23.2%)	50 (22.6%)	59 (23.7%)
	6 to 10	23 (4.9%)	10 (4.5%)	13 (5.2%)
	More than 10	19 (4.0%)	6 (2.7%)	13 (5.2%)
	Not stated	11 (2.3%)	8 (3.6%)	3 (1.2%)

STI: sexually transmitted infection

[1]Counselling centers: Fixpunkt e.V., Mann-o-Meter e.V., Berliner AIDS-Hilfe e.V., Pluspunkt / Schwulenberatung Berlin GmbH (listed in descending order according to the number of questionnaires returned

[2]Practices: Gemeinschaftspraxis Dietmar Schranz und Klaus Fischer, Praxis Jessen[2] + Kollegen, Praxis Wünsche, Ärztezentrum Nollendorfplatz, Praxiszentrum Kaiserdamm, Novopraxis Berlin GbR (listed in descending order according to number of questionnaires returned

*or similar

**for example: A levels, high school diploma, German "Abitur"

Barriers to PrEP Usage

When asked if participants perceived PrEP as a safe way to prevent HIV infection, two-thirds (65.6%) of respondents agreed (18). Among participants who reported greater knowledge of PrEP, agreement was significantly more common (p<0.001) (18). When given a list of perceived risks to using PrEP with multiple answers allowed, respondents attributed the following to PrEP use: a higher risk of infection with other STIs (64.3%), mild or temporary side effects (43.6%), severe or permanent side effects (19.8%), a higher risk of HIV infection (6.2%) and other risks (5.1%) (18). After applying a Bonferroni-adjusted alpha-level (p<0.005) to account for multiple comparisons across survey items, the only significant differences between well-informed respondents and ill-informed respondents were in the "higher risk of getting infected with other STIs and "not sure" (***Table 4***) (18).

Desire to use and Likelihood of Using PrEP

PrEP-naïve respondents (n=387, 42.4%) indicated that they would like to use PrEP ("strongly agree" or "agree"); however, over a third of respondents showed no interest in beginning PrEP ("strongly disagree" or "disagree) (18). We performed a logistic regression model to ascertain predictive factors associated with an interest in taking PrEP, and the following were significant: (1) belonging to a higher-risk sexual risk behavior group (higher risk (CAI)" or "highest risk (CAI + STI)"), (2) perceiving their own sexual behavior as risk, and (3) expressing the need to find a physician to prescribe them PrEP (18). A negative predictive factor for interest in PrEP initiation was found to be perceiving PrEP use to contribute to an increased risk of contracting STIs (18). Our multivariable regression model indicated two positive predictive factors for PrEP initiation interest: (1) belonging to a higher risk sexual behavior group ("higher risk (CAI)" or "highest risk (CAI + STI)") and (2) expressing the need for a doctor who

prescribes PrEP (18). The single negative predictive factor for PrEP use in the multivariate analysis was attributing PrEP use to a higher risk of contracting STIs (18).

Table 4. ORs and 95% Confidence Intervals for expressing a desire to use PrEP according to sexual risk behavior, perceived riskiness of participants' own sexual behavior and perceived barriers and risks to PrEP use (18).

		Participants expressing a desire to use PrEP		Crude OR	Adjusted OR[†]
Participant characteristics	**N[‡]**	**n (%)**	***p*-value[§]**	**(95% CI)**	**(95% CI)**
Sexual risk behavior (past six months)			<0.001		
No STI; no multiple** CAI partners	193	86 (44.6%)		Reference	Reference
STI; no multiple** CAI partners	17	7 (41.2%)		0.85 (0.31 – 2.33)	1.02 (0.34 – 3.05)
No STI; multiple** CAI partners	66	52 (78.8%)		4.58 (2.33 – 9.00)	3.77 (1.84 – 7.69)
STI; multiple** CAI partners	20	19 (95.0%)		23.07 (3.03– 175.93)	17.22 (2.18– 136.14)
Perceived riskiness of own sexual behavior: "When I have sex, it is always as safe as I'd like it to be"			<0.001		
Strongly disagree	9	6 (66.7%)		Reference	Reference
Disagree	51	39 (76.5%)		1.27 (0.22 – 7.39)	2.16 (0.4 – 11.64)
Neither agree nor disagree	37	27 (73.0%)		1.16 (0.19 – 7.04)	2.63 (0.46 – 14.94)
Agree	123	64 (52.0%)		0.44 (0.08 – 2.37)	1.31 (0.26 – 6.44)
Strongly agree	73	27 (37.0%)		0.23 (0.04 – 1.28)	0.77 (0.15 – 3.90)
"If a doctor prescribed it"			0.012		
Not selected as a circumstance under which a participant would use PrEP	202	99 (49.0%)		Reference	Reference
Selected as a circumstance under which the participant would use PrEP	97	65 (67.0%)		1.96 (1.17 – 3.28)	2.44 (1.36 – 4.37)
"A higher risk of getting infected with HIV"			0.078		
Not selected as risk seen for people using PrEP	282	158 (56.0%)		Reference	Reference
Selected as a risk for people using PrEP	16	5 (31.3%)		0.38 (0.13 – 1.14)	0.34 (0.10 – 1.11)
"A higher risk of getting infected with other STIs"			0.053		
Not selected as risk seen for people using PrEP	120	76 (63.3%)		Reference	Reference
Selected as a risk for people using PrEP	178	87 (48.9%)		0.53 (0.32 – 0.87)	0.54 (0.31 – 0.92)

Legend: *CAI, condomless anal intercourse, CI, confidence interval; OR, odds ratio; PrEP, HIV pre-exposure prophylaxis; STI, sexually transmitted infection.*

P-values from joint Wald tests of the null hypothesis that there is no variation across a category for the univariate and multivariate regression models were <0.0001 and 0.0002 for sexual risk behavior; <0.0001 and 0.0576 for perceived riskiness of participants' own sexual behavior; 0.0095 and 0.0028 for doctor prescription as a pre-condition for PrEP use; 0.074 and 0.0748 for attributing to PrEP a higher risk of getting infected with HIV; and 0.0105 and 0.0243 for attributing to PrEP a higher risk of getting infected with other STIs, respectively.

[†] Multivariable analysis for adjusting for sexual risk behavior, perceived riskiness of participants' own sexual behavior, having a doctor who prescribes PrEP and risk of HIV and STI infection attributed to PrEP intake.

[‡] The sample excludes patients who were missing information on the relevant variables.

[§] From the Chi-squared tests of the null hypothesis that there is no significant difference between the expected frequencies and the observed frequencies in one or more categories (e.g. across sexual risk behavior groups)

** "Multiple" was defined as reporting having had two or more CAI partners in the past six months

History of PrEP use and PrEP sourcing

The vast majority of respondents (82.3%) had never used PrEP, and the 81 (17.2%) respondents who had used PrEP before reported a range of intake options, largely continuous use (46.9%), previous but irregular usage (39.5%), and lastly on-demand use (13.6%) (18). Regarding sourcing, respondents were allowed to choose multiple answers, and the many respondents did receive PrEP as a private prescription from a physician (44.4%) (18). The majority of respondents, however, reported informal PrEP sourcing via either imports from another country (35.8%), using pills originally prescribed for PEP (post-exposition prophylaxis) (18.5%), using a friend's HIV medication (11.1%) or another method (4.9%) (18). When asked how they source PrEP, only a third (32.1%) of respondents indicated they solely sourced PrEP via a private prescription, while the vast majority (59.3%) reported sourcing at least some to all of their PrEP via informal, non-direct prescription-based channels (18).

Variables positively associated with having had previously taken PrEP included: (1) having a university degree, (2) having been born outside of Germany, (3) belonging to the "higher risk (CAI)" or "highest risk (CAI + STI)" risk categories, (4) having friends or acquaintances who are living with HIV, and (5) attributing a higher rate of STI infection with PrEP use (18). Our multivariate analysis, positive predictive factors for future PrEP use included: (1) belonging to the "higher risk (CAI)" or "highest risk (CAI + STI)" sexual risk categories, (2) having a university degree, (3) having one or two parents born outside of Germany, (4) having friends or acquaintances living with HIV, and (5) attributing a higher risk of STI infection with PrEP use (18).

Anticipated Impact on Condom Usage

When asked about whether they agreed with the following statement: "I have (or would have) anal sex without a condom more often when taking PrEP", nearly half of participants (45.4%) either agreed or strongly agreed; however, a third of respondents (33.0%) disagreed or strongly disagreed (18). Respondents who were currently or had previously taken PrEP were more likely to agree with the aforementioned statement than participants without a history of PrEP or an intention to take PrEP (18).

Table 5. Anticipated impact of PrEP on participants' condom usage, according to desire to use PrEP and history of PrEP use (18)

"I have (or would have) anal sex without a condom more often when taking PrEP"						
	"I would like to use PrEP myself"		**p-value***	***History of PrEP use***		**p-value***
	Agree or strongly Agree (N= 207)	**Neutral, disagree or strongly disagree (N=211)**		**Yes (N=80)**	**No (N=372)**	
Strongly disagree	18 (8.7%)	58 (27.5%)	< 0.001	7 (8.8%)	77 (20.7%)	0.002
Disagree	36 (17.4%)	32 (15.2%)		7 (8.8%)	64 (17.2%)	
Neither agree nor disagree	23 (11.1%)	38 (18.0%)		8 (10.0%)	55 (14.8%)	
Agree	79 (38.2%)	64 (30.3%)		37 (46.3%)	116 (31.2%)	
Strongly agree	39 (18.8%)	13 (6.2%)		17 (21.3%)	42 (11.3%)	
I never use condoms anyway	12 (5.8%)	6 (2.8%)		4 (5.0%)	18 (4.8%)	

*From Chi-squared tests of the null hypothesis that there is no significant difference between the expected frequencies and the observed frequencies in the categories.

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All demographic data are shown in ***Table 6***. The mean age of participants was 46.0 years (SD = 11.7) (19). 76 participants (52.4%) identified as male, 61 participants (42.1%) identified as female, and two participants (1.4%) identified as gender non-binary (19). The majority of participants had primary professional qualifications in social work (n = 93, 64.1%) (19). The rest of the participants had qualifications as physicians (n = 15, 10.3%), psychologists (n = 14, 9.7%) or nurses (n = 4, 2.8%) (19). A majority of respondents worked in counseling centers in large cities of more than 100,000 inhabitants (n = 89, 61.4%) or in a major city of more than 1,000,000 inhabitants (n = 43, 29.7%) (19). The vast majority of respondents (n = 123, 84.8%) worked in one of the older German states (previously known as West Germany) including the city state of Berlin (19). Statistically significant associations were found between the type of center and the following demographic data: gender ($\chi 2$ (df = 2, n = 139) = 17,40, $p < 0.001$) and primary professional qualification ($\chi 2$ (df = 4, n = 139) = 19,85, $p = 0.001$) (19).

Table 6. *Demographic data and contextual characteristics of the study sample (19)*

Variable	**Total Sample**		**Type of Center**				
			Local health offices		**NG counselling centers**		
N	145		56		89		
Age in years (*n = 139*)							*p* = 0.679*
Mdn (IQR)	48.00	(19.00)	48.00	(17.00)	47.50	(21.75)	
M (SD)	46.03	(11.67)	46.51	(11.51)	45.75	(11.82)	
Min; Max	19 – 67		19 – 62		23 – 67		
Gender (*n, %*)							p < 0.001†
Female	61	(42.1%)	34	(60.7%)	27	(30.3%)	
Male	76	(52.4%)	17	(30.4%)	59	(66.3%)	
Non-binary	2	(1.4%)	0	(0.0%)	2	(2.2%)	
Not specified	6	(4.1%)	5	(8.9%)	1	(1.1%)	
Professional qualification (*n, %*)							*p = 0.001†*
Social work	93	(64.1%)	37	(66.1%)	56	(62.9%)	
Psychology	14	(9.7%)	2	(3.6%)	12	(13.5%)	
Nursing	4	(2.8%)	1	(1.8%)	3	(3.4%)	
Physician	15	(10.3%)	11	(19.6%)	4	(4.5%)	
Other	13	(9.0%)	0	(0.0%)	13	(14.6%)	
Not specified	6	(4.1%)	5	(8.9%)	1	(1.1%)	
Size of the location (*n, %*)							*p* = 0.138*
Major city (>1,000,000)	43	(29.7%)	15	(26.8%)	28	(31.5%)	
Large city (>100,000)	89	(61.4%)	31	(55.4%)	58	(65.2%)	
City (>10,000)	7	(4.8%)	5	(8.9%)	2	(2.2%)	
Small city (≤ 10,000)	1	(0.7%)	1	(1.8%)	0	(0%)	
Not specified	5	(3.4%)	4	(7.1%)	1	(1.1%)	
Federal state (*n, %*)							*p = 0.072†*
Baden-Wuerttemberg	20	(13.8%)	3	(5.4%)	17	(19.1%)	
Bavaria	22	(15.2%)	8	(14.3%)	14	(15.7%)	
Berlin	15	(10.3%)	7	(12.5%)	8	(9.0%)	
Brandenburg	9	(6.2%)	3	(5.4%)	6	(6.7%)	
Bremen	1	(0.7%)	0	(0.0%)	1	(1.1%)	
Hamburg	13	(9.0%)	4	(7.1%)	9	(10.1%)	
Hesse	12	(8.3%)	2	(3.6%)	10	(11.2%)	
Mecklenburg – Western Pomerania	2	(1.4%)	2	(3.6%)	0	(0.0%)	
Lower Saxony	8	(5.5%)	6	(10.7%)	2	(2.2%)	
North Rhine-Westphalia	22	(15.2%)	8	(14.3%)	14	(15.7%)	
Rhineland-Palatinate	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Saarland	4	(2.8%)	3	(5.4%)	1	(1.1%)	
Saxony	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Saxony-Anhalt	1	(0.7%)	0	(0.0%)	1	(1.1%)	
Schleswig-Holstein	6	(4.1%)	3	(5.4%)	3	(3.4%)	
Thuringia	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Not specified	10	(6.9%)	7	(12.5%)	3	(3.4%)	
Professional experience in years (*n* = 138)							*p* = 0.838†
Median (IQR)	11.50	(18.25)	11.0	(17.50)	12.00	(19.75)	
Mean (*SD*)	14.19	(10.38)	14.14	(10.02)	14.23	(10.63)	
Min – Max	0.5 – 40.0		0.5 – 31.0		1 – 40.0		

Legend: *IQR,* interquartile range; *M,* mean; *Max,* maximum; *Mdn,* Median; *Min,* Minimum; *SD,* Standard deviation. * From Mann-Whitney U tests of the null hypothesis that the median value of the participants from local health offices is equal to that of participants form NG counselling centers. † From Pearson's Chi-squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, according to type of counselling center.

Counselling Sessions and Advising Practices

The information regarding counselling sessions and HIV testing practices is listed in ***Table 7***. On average, counsellors noted 36.6 sessions with MSM and transgender persons per month (*SD* = 48.2) and 16.0 sessions with "at risk" MSM and transgender persons who could benefit from taking PrEP (*SD* = 22.2) (19). We saw no significant differences regarding the frequency of sessions with MSM and transgender persons or at-risk persons between NG counselling centers and LHOs; although, counsellors from LHOs reported a higher frequency of HIV tests performed each month (*Median* = 180, *IQR* = 190) than participants from NG counselling centers (*Median* = 47.5, *IQR* = 73.8), *U* = 1103.5, *p* < 0.001 (19). The absolute or relative number of positive HIV tests performed each month, however, was insignificant between the two groups (19).

Table 7. Counselling sessions and HIV testing (19)

Variable	Total Sample		Type of Center				
			Local Health Office		NG counselling center		
Number of overall counseling sessions with MSM and trans persons per month (*n* = 126)							*p* = 0.784*
Median (IQR)	20.00	(35.00)	20.00	(40.00)	25.00	(30.00)	
Mean (*SD*)	36.55	(48.23)	39.21	(52.13)	34.96	(46.03)	
Min – Max	0 – 330		0 – 270		0 – 330		
Number of sessions with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guidelines (at-risk clients) (*n* = 116)							*p* = 0.780*
Median (IQR)	10.00	(10.00)	10.00	(12.50)	10.00	(10.00)	
Mean (*SD*)	15.97	(22.17)	15.38	(18.70)	16.35	(24.23)	
Min – Max	0 – 170		0 – 80		1-170		
Overall number of HIV tests run per month (*n* = 123)							*p* < 0.001*
Median (IQR)	60.00	(175.00)	180.00	(190.00)	47.50	(73.75)	
Mean (*SD*)	112.69	(109.85)	162.81	(116.12)	81.70	(93.87)	
Min – Max	3 – 400		3 – 400		8 – 350		
Number of positive HIV tests per month (*n* = 117)							*p* = 0.311*
Median (IQR)	0.00	(1.00)	1.00	(1.00)	0.00	(1.00)	
Mean (*SD*)	0.67	(0.83)	0.78	(0.90)	0.60	(0.78)	
Min – Max	0 – 4		0 – 3		0 – 4		
Proportion of positive HIV test results per overall number of HIV tests run per month (*n* = 117)							*p* = 0.373*
Median (IQR)	0.00%	(0.93)	0.33%	(0.65)	0.00%	(1.67)	
Mean (*SD*)	0.74%	(1.49)	0.34%	(0.38)	0.99%	(1.84)	
Min – Max	0 – 12.5%		0 – 1.25%		0 – 12.5%		

Legend: *IQR,* interquartile range; *M,* mean; *Max,* maximum; *Mdn,* Median; *Min,* Minimum; *SD,* Standard deviation. * From Mann-Whitney U tests of the null hypothesis that the median value of participants from local health offices is equal to that of participants from NG counselling centers.

Across the entire sample, respondents noted that, during an average of 26.1% of sessions with at-risk clients, the clients themselves engaged the participants in conversations about PrEP (*SD* = 22.0). The proportion of proactive PrEP advisement averaged 52.0% across both counselling groups (*SD* = 34.2). Clients more frequently broached the topic of PrEP themselves in sessions with NG counsellors (*Median* = 30.0%, *IQR* = 40.0) than with LHO counsellors (*Median* = 10.0%, *IQR* = 10.0), *U* = 877.0, $p < 0.001$. When reviewing the proportion of proactive PrEP advisement among counsellors, NG counsellors also more frequently actively broached the topic of PrEP (*Median* = 50.0%, *IQR* = 60.0) than LHO counsellors (*Median* = 30.0%, *IQR* = 70.0), *U* = 1082.0, $p = 0.003$. Data are depicted in ***Table 8***.

Table 8. Counselling practice in counselling sessions with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guidelines ("at-risk clients") (19)

Variable	Total Sample		Type of Center				
			Local Health Office		NG counselling center		
Proportion of sessions with 'at-risk' MSM and trans persons in which the topic PrEP is addressed by the clients themselves (*n* = 115)							$p < 0.001$*
Median (IQR)	20.00%	(30.00)	10.00%	(10.00)	30.00%	(40.00)	
Mean (*SD*)	26.09%	(21.95)	16.36%	(15.86)	32.11%	(23.11)	
Min – Max	0 – 100%		0 – 80%		0 – 100%		
Proportion of sessions with 'at-risk' MSM and trans persons in which the counselors themselves proactively address the topic PrEP (*n* = 116)							$p = 0.003$*
Median (IQR)	50.00%	(70.00)	30.00%	(70.00)	50.00%	(60.00)	
Mean (*SD*)	51.98%	(34.24)	41.33%	(36.72)	58.73%	(30.98)	
Min – Max	0 – 100%		0 – 100%		10 – 100%		

Legend: *IQR,* interquartile range; *Max,* maximum; *Min,* Minimum; *SD,* Standard deviation. * From Mann-Whitney U tests of the null hypothesis that the median value of participants from local health offices is equal to that of participants from NG counselling centers.

Self-assessment of PrEP knowledge and counselling competencies

Participants from both types of counselling centers most frequently agreed with all of the statements assessing PrEP knowledge and counselling competency, indicating a

positive self-assessment (19). There was, however, a statistically significant difference in the frequency of agreement across all of the listed statements between LHO counsellors and NG counsellors (*see* ***Table 9***) (19). The summative knowledge score (Cronbach's alpha = 0.966) summarizes these findings with the knowledge score of LHO counsellors being significantly lower (*Median* = 14.0, *IQR* = 4.0) than NG counsellors (*Median* = 18.0, *IQR* = 5.0), $U = 679.5$, $p < 0.001$ (19).

Table 9. Self-assessment of knowledge and counselling competence (19)

Variable	Total Sample		Type of Center				
			Local Health Office		NG counselling center		
Global assessment: "I am well-informed about PrEP" (*n, %*), *n* = 113							$p < 0.001^{\dagger}$
Strongly disagree	1	(0.9%)	0	(0.0%)	1	(1.4%)	
Disagree	2	(1.8%)	1	(2.3%)	1	(1.4%)	
Neither agree nor disagree	13	(11.5%)	11	(25.0%)	2	(2.9%)	
Agree	44	(38.9%)	21	(47.7%)	23	(33.3%)	
Strongly agree	53	(46.9%)	11	(25.0%)	42	(60.9%)	
Indications: "I am able to comprehensively give clients advice on whether it makes sense to take PrEP in their respective case" (*n, %*), *n* = 113							$p < 0.001^{\dagger}$
Strongly disagree	1	(0.9%)	0	(0.0%)	1	(1.4%)	
Disagree	6	(5.3%)	5	(11.6%)	1	(1.4%)	
Neither agree nor disagree	9	(8.0%)	5	(11.6%)	4	(5.7%)	
Agree	38	(33.6%)	22	(51.2%)	16	(22.9%)	
Strongly agree	59	(52.2%)	11	(25.6%)	48	(68.6%)	
Adverse effects: "I am able to comprehensively give clients advice on the adverse effects of PrEP" (*n, %*), *n* = 113							$p < 0.001^{\dagger}$
Strongly disagree	3	(2.7%)	2	(4.7%)	1	(1.4%)	
Disagree	11	(9.7%)	8	(18.6%)	3	(4.3%)	
Neither agree nor disagree	26	(23.0%)	16	(37.2%)	10	(14.3%)	
Agree	37	(32.7%)	11	(25.6%)	26	(37.1%)	
Strongly agree	36	(31.9%)	6	(14.0%)	30	(42.9%)	
Modalities of intake: "I am able to comprehensively give clients advice on the possible modalities of intake of PrEP (e.g., continuous vs. on-demand)" (*n, %*), *n* = 113							$p < 0.001^{\dagger}$
Strongly disagree	2	(1.8%)	1	(2.3%)	1	(1.4%)	
Disagree	13	(11.5%)	11	(25.6%)	2	(2.9%)	
Neither agree nor disagree	8	(7.1%)	3	(7.0%)	5	(7.1%)	
Agree	35	(31.0%)	20	(46.5%)	15	(21.4%)	
Strongly agree	55	(48.7%)	8	(18.6%)	47	(67.1%)	
Investigations: "I am able to comprehensively give clients advice on the medical investigations necessary during the use of PrEP" (*n, %*), *n* = 113							$p = 0.002^{\dagger}$
Strongly disagree	3	(2.7%)	2	(4.7%)	1	(1.4%)	
Disagree	10	(8.8%)	8	(18.6%)	2	(2.9%)	
Neither agree nor disagree	10	(8.8%)	4	(9.3%)	6	(8.6%)	
Agree	37	(32.7%)	18	(41.9%)	19	(27.1%)	
Strongly agree	53	(46.9%)	11	(25.6%)	42	(60.0%)	
Knowledge score (0-20), *n* = 112							$p < 0.001^{*}$
Median (IQR)	17.00	(6.00)	14.00	(4.00)	18.00	(5.00)	
Mean (*SD*)	15.64	(4.43)	13.30	(4.38)	17.10	(3.82)	
Min – Max	0 – 20		4 – 20		0 - 20		

Legend: *IQR,* interquartile range; *Max,* maximum; *Min,* Minimum; *SD,* Standard deviation. * From Mann-Whitney U tests of the null hypothesis that the median value of the participants from local health offices is equal to that of participants form NG

counselling centers. † From Pearson's Chi-squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, according type of counselling center.

Attitudes towards PrEP

Mirroring the previously assessed knowledge sore, participants more frequently agreed (and therefore responded more positively) than disagreed or were indifferent to the positive statements regarding PrEP (19). The one negative statement about PrEP was met with disagreement more frequently than indifference or agreement (19). Between the two counselling groups, the summative attitude score (Cronbach's alpha = 0.847) was higher among NG counsellors (Median = 18.0, IQR = 4.0) than LHO counsellors (*Median* = 14.0, *IQR* = 6.8), $U = 638.5$, $p < 0.001$(19).

Table 10. Attitudes towards PrEP (19)

Variable	Total Sample		Type of Center				
			Local Health Office		NG counselling center		
Global assessment: "I think that PrEP is an important element of HIV prevention strategies" (*n, %*), *n* = 114							$p < 0.001^{\dagger}$
Strongly disagree	1	(0.9%)	1	(2.3%)	0	(0.0%)	
Disagree	2	(1.8%)	2	(4.5%)	0	(0.0%)	
Neither agree nor disagree	11	(9.6%)	8	(18.2%)	3	(4.3%)	
Agree	16	(14.0%)	13	(29.5%)	3	(4.3%)	
Strongly agree	84	(73.7%)	20	(45.5%)	64	(91.4%)	
Reliability: "I think that PrEP is a reliable method to protect oneself from HIV" (*n, %*), *n* = 114							$p = 0.003^{\dagger}$
Strongly disagree	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Disagree	6	(5.3%)	4	(9.1%)	2	(2.9%)	
Neither agree nor disagree	7	(6.1%)	5	(11.4%)	2	(2.9%)	
Agree	33	(28.9%)	18	(40.9%)	15	(21.4%)	
Strongly agree	68	(59.6%)	17	(38.6%)	51	(72.9%)	
Adverse effects: "I think that PrEP is a method to protect oneself from HIV that has few side effects" (*n, %*), *n* = 114							$p = 0.002^{\dagger}$
Strongly disagree	8	(7.0%)	3	(6.8%)	5	(7.1%)	
Disagree	12	(10.5%)	8	(18.2%)	4	(5.7%)	
Neither agree nor disagree	32	(28.1%)	18	(40.9%)	14	(20.0%)	
Agree	32	(28.1%)	11	(25.0%)	21	(30.0%)	
Strongly agree	30	(26.3%)	4	(9.1%)	26	(37.1%)	
Availability of better alternatives: "I think that PrEP is unnecessary, because there are better alternatives to protect oneself from HIV" (*n, %*), *n* = 114							$p < 0.001^{\dagger}$
Strongly disagree	67	(58.8%)	14	(31.8%)	53	(75.7%)	
Disagree	30	(26.3%)	18	(40.9%)	12	(17.1%)	
Neither agree nor disagree	11	(9.6%)	7	(15.9%)	4	(5.7%)	
Agree	5	(4.4%)	4	(9.1%)	1	(1.4%)	
Strongly agree	1	(0.9%)	1	(2.3%)	0	(0.0%)	
Reimbursement of costs: "I think that PrEP should be paid for by the statutory health insurance" (*n, %*), *n* = 114							$p < 0.001^{\dagger}$
Strongly disagree	8	(7.0%)	5	(11.4%)	3	(4.3%)	
Disagree	9	(7.9%)	6	(13.6%)	3	(4.3%)	
Neither agree nor disagree	16	(14.0%)	13	(29.5%)	3	(4.3%)	
Agree	22	(19.3%)	9	(20.5%)	13	(18.6%)	
Strongly agree	59	(51.8%)	11	(25.0%)	48	(68.6%)	
Knowledge score (0-20), *n* = 112							$p < 0.001^{*}$
Median (IQR)	17.50	(5.00)	14.00	(6.75)	18.00	(4.00)	
Mean (*SD*)	15.96	(4.01)	13.57	(4.16)	17.46	(3.10)	
Min – Max	4-20		4-20		7-20		

Legend: *IQR,* interquartile range; *Max,* maximum; *Min,* Minimum; *SD,* Standard deviation. * From Mann-Whitney U tests of the null hypothesis that the median value of the participants from local health offices is equal to that of participants form NG counselling centers. † From Pearson's Chi-squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, according to type of counselling center.

Multiple Linear Regression of the Proportion of Proactive PrEP Advisement

We developed a multiple linear regression model to predict the proportion of counsellors' proactive PrEP advisement to at-risk clients (19). We applied a backwards elimination method with p <0.2 as a stopping rule for variable exclusion, and a significant regression was found (F(2,109) = 10.50, p<0.001, n=112), with R^2 = 0.162 (see ***Table 11***) (19). The only remaining independent predictive factors were the knowledge and attitude scores (19). The proportion of proactively provided PrEP advice increased by 1.7% for each point increase in knowledge score and by 2.1% for each point increase in attitudes score (19).

Table 11. Multiple linear regression analysis to predict the proportion of PrEP advice provided proactively to MSM and trans persons who meet the criteria to be offered PrEP according to the German and Austrian guidelines ("at-risk clients") (19)

Predictors	Coefficient (Robust SE)		Beta	*p*	VIF
Constant	- 8.208	(11.468)		0.476	
Knowledge score*	1.692	(0.842)	0.221	0.047	1.26
Attitudes score**	2.111	(0.910)	0.250	0.022	1.26

Legend: *SE,* standard error; *VIF,* variance inflation factor. *Scale from 0 to 20 points, with higher values indicating a more positive self-assessment of knowledge about PrEP and counselling competence. **Scale from 0 to 20 points, with higher values indicating a more positive attitude towards PrEP.

Educational Materials

Less than half of participants (n=55, 48.7%) indicated that an in-house PrEP guideline or standard operating procedure (SOP) existed within their organization, and a large majority of participants responded that they had been offered PrEP training (n =98, 86.0%). Less than half of participants wanted to receive further training on PrEP counselling techniques (n = 50, 44.6%). Although not statistically significant (χ^2(df = 1, n = 114) = 2,447, p = 0.118), NG counsellors were more frequently offered PrEP training advice (n = 63, 90.0%) than LHO counsellors (n = 35, 79.5%). Furthermore,

no significant difference between counsellor groups was noted in the availability of in-house guidelines or desire for further PrEP training. When asked what educational materials or training could improve counselling practices, respondents most frequently chose decision aids for clients in client-friendly language and in different languages (both: *n* = 89, 78.8%), followed by a clinical practice guideline with an overview of indications, contraindications and necessary testing (*n* = 84, 74.3%). Least frequently chosen were app- or SMS-based reminder services for PrEP users to help promote adherence (*n* = 66, 58.4%), information for counsellors on managing PrEP (*n* = 51, 45.1%), information and/or training for counsellors on identifying PrEP candidates (*n* = 43, 38.1%) and information for counsellors on broaching the topic of sexuality with clients (*n* = 32, 28.3%).

Counsellor-perceived Barriers to PrEP initiation

When respondents were asked to rate a list of barriers for PrEP candidates to initiating PrEP, respondents noted clients' worries about getting infected with other STIs (*Mean* = 5.56, *SD* = 2.73), the costs of taking PrEP (*Mean* = 5.33, *SD* = 2.61), and a lack of PrEP in clients' native language (*Mean* = 5.10, *SD* = 3.33).

Table 12. Counsellor-perceived barriers to PrEP initiation (19)

Barrier	***n***	***Mean***	***(SD)***
Patient-associated Barriers			
Worries about getting infected with other STIs	111	5.56	(2.73)
Monthly costs of PrEP treatment	109	5.33	(2.61)
Lack of information about PrEP in clients' native languages	110	5.10	(3.33)
Costs for the bloodwork	109	4.80	(3.00)
Worries about mild or temporary side effects	109	4.64	(2.43)
Time required for regular visits to the doctor	111	4.26	(2.81)
Worries about severe or permanent side effects	111	4.21	(2.59)
Lack of information about PrEP in client-friendly language	110	4.17	(2.88)
Difficulties in finding a doctor who prescribes PrEP	112	4.13	(3.64)
Assessment of their own risk of getting infected with HIV as too low to take PrEP	110	4.08	(2.70)
Worries stigmatization in the peer group	107	3.33	(2.67)
Cultural barriers	110	2.79	(2.51)

Legend: *n*, number; *IQR*, interquartile range

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After excluding seven responses due to lack of meaningful information, a total of 154 respondents were included in our analyses(20). 72 practiced in HIV-specialty clinics, and 79 worked in non-HIV-specialty practices; three did not provide any information on their specialty status or their practice location and were only included in barrier and training analyses (20). All demographic data are shown in ***Table 13***. Statistically significant associations were found between HIV specialty status and gender (χ^2(*df* = 1, *n* = 151) = 6.938, *p* = 0.008), specialty (χ^2 (*df* = 5, *n* =151) = 83.379, *p* <0.001), size of the practice's location (χ^2(*df* = 3, n = 142) = 33.378, *p* <0.001), and also the state in which the practice is located (i.e. previous eastern vs western states) (χ^2 (*df* = 1, *n* = 151) = 3.833, *p* = 0.05) (20).

Table 13. Demographic data and contextual characteristics of the sample. (20)

Variable	**Total Sample**		**HIV Specialist Status**				
			HIV Specialists		**Non-HIV Specialists**		
N	154		72		79		
Age in years (*n = 145*)							*p = 0.180*[†]
Mean (SD)	52.22	(8.98)	51.20	(8.46)	53.20	(9.39)	
Min; Max	33-84		34-76		33-84		
Gender (*n, %*)							p = 0.008[§]
Female	54	(35.1%)	18	(25.0%)	36	(45.6%)	
Male	97	(63.0%)	54	(75.0%)	43	(54.4%)	
Not specified	3	(1.9%)	0	(0.0%)	0	(0.0%)	
Specialty (*n, %*)							*p < 0.001*[§]
General Medicine	35	(22.7%)	11	(15.3%)	24	(30.4%)	
Internal Medicine	27	(17.5%)	22	(30.6%)	5	(6.3%)	
Dermatology	25	(16.2%)	4	(5.6%)	21	(26.6%)	
Urology	25	(16.2%)	0	(0.0%)	25	(31.6%)	
General Medicine and Internal Medicine with Additional Qualification for Infectious Disease	37	(24.0%)	35	(48.6%)	2	(2.5%)	
Not specified	5	(3.4%)	0	(0.0%)	2	(2.5%)	
Size of the city (n, %)							*p < 0.001*[§]
Major city (>1,000,000)	52	(33.8%)	36	(50.0%)	16	(20.3%)	
Large city (>100,000)	44	(28.6%)	25	(34.7%)	19	(24.1%)	
City (>10,000)	27	(17.5%)	4	(5.6%)	23	(29.1%)	
Small city (≤ 10,000)	19	(12.3%)	2	(2.8%)	17	(21.5%)	
Not specified	12	(7.8%)	5	(6.9%)	4	(5.1%)	
Federal state (n, %)							*p = 0.05*[#]
Western German states, including Berlin	**123**	**(79.9%)**	**62**	**(86.1%)**	**61**	**(77.2%)**	
Baden-Württemberg	15	(9.7%)	8	(11.1%)	7	(8.9%)	
Bavaria	18	(11.7%)	13	(18.1%)	5	(6.3%)	
Berlin	26	(16.9%)	14	(19.4%)	12	(15.2%)	
Bremen	2	(1.3%)	0	(0%)	2	(2.5%)	
Hamburg	5	(3.2%)	4	(5.6%)	1	(1.3%)	
Hesse	23	(14.9%)	12	(16.7%)	11	(13.9%)	
Lower Saxony	5	(3.2%)	0	(0.0%)	5	(6.3%)	
North Rhine-Westphalia	22	(14.3%)	10	(13.9%)	12	(15.2%)	
Rhineland-Palatinate	5	(3.2%)	1	(1.4%)	4	(5.1%)	
Saarland	2	(1.3%)	0	(0.0%)	2	(2.5%)	
Schleswig-Holstein	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Eastern German states, excluding Berlin	**19**	**(12.3%)**	**5**	**(6.9%)**	**14**	**(17.7%)**	
Brandenburg	2	(1.3%)	0	(0.0%)	2	(2.5%)	
Mecklenburg-Western Pomerania	1	(0.6%)	0	(0.0%)	1	(1.3%)	
Saxony	7	(4.5%)	3	(4.2%)	4	(5.1%)	
Saxony-Anhalt	5	(3.2%)	0	(0.0%)	5	(6.3%)	
Thuringia	4	(2.6%)	2	(2.8%)	2	(2.5%)	
Not specified	12	(7.8%)	5	(6.9%)	4	(5.1%)	

Legend: *Max*, maximum; *Min*, minimum; *SD*, standard deviation; *3 patients who were included in some of the analyses in the present study did not provide information about their specialist status (HIV-specialists vs. non-HIV-specialists); †From independent samples t-tests of the null hypothesis that the mean value of non-HIV-specialists is equal to that of HIV specialists; §From Pearson's Chi squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, according to the HIV specialist status; #From Pearson's Chi squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in the categories "western German states" vs. "eastern German states", according to the HIV specialist status.

Physician appointments with "at-risk" patients and HIV testing practices

Table 14 indicates the data on the number of appointments with MSM and transgender patients, as well as the HIV testing experience of the physicians' practices (20). Additionally, the frequency of HIV PrEP prescriptions written for patients who meet the criteria to be offered PrEP and the proportion of patients receiving prescriptions to those who meet the criteria to receive one are listed in ***Table 15***.

Table 14. Number of appointments with different categories of patients and HIV-tests per calendar quarter (20)

Variable	Total Sample		HIV Specialist Status				
			HIV Specialists		Non-HIV Specialists		
Number of overall appointments with MSM and trans persons per quarter (*n* = 141)							*p < 0.001*†
Median (IQR)	30.0	(345.0)	375.0	(400.0)	5.0	(18.0)	
Mean (*SD*)	162.50	(213.05)	327.88	(210.47)	16.97	(33.20)	
Q1 – Q3	5.0 - 350.0		100.0 – 500.0		2.0 – 20.0		
Number of appointments with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guideline (at-risk clients) per quarter (*n* = 131)							*p < 0.001*†
Median (IQR)	17.0	(99.0)	100.0	(170.0)	1.0	(6.0)	
Mean (*SD*)	71.74	(114.08)	143.60	(132.33)	7.17	(15.33)	
Q1 – Q3	1.0 – 100.0		30.0 – 200.0		0.0 – 6.0		
Overall number of HIV tests per quarter (*n* = 145)							*p < 0.001*†
Median (IQR)	20.0	(87.0)	80.0	(195.0)	4.0	(17.7)	
Mean (*SD*)	73.14	(124.03)	139.94	(152.79)	12.50	(23.21)	
Q1 – Q3	3.0 – 90.0		30.0 – 225.0		1.0 – 18.7		
Number of positive HIV test results per quarter (*n* = 143)							*p < 0.001*†
Median (IQR)	1.0	(2.0)	2.0	(4.0)	0.0	(1.0)	
Mean (*SD*)	5.64	(30.46)	11.45	(43.93)	0.51	(1.36)	
Q1 – Q3	0.0 – 2.0		1.0 – 5.0		0.0 – 1.0		
Number of MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guideline (at-risk clients) who received a prescription for PrEP per quarter (*n* = 131)							*p < 0.001*§
Median (IQR)	3.0	(40.0)	40.0	(67,5)	0.00	(1.0)	
Mean (*SD*)	28.14	(56.25)	59.25	(70.72)	1.03	(3.26)	
Q1 – Q3	0.0 – 40.0		15.0 – 82.5		0.0 – 0.0		
Proportion of guideline-meeting patients who receive a prescription for PrEP per total number of guideline-meeting patients, (*n* = 108)							*p < 0.001*§
Median (IQR)	23.10%	(57.5%)	50.00%	(50.0%)	0.00%	(4.17%)	
Mean (*SD*)	31.25%	(32.05%)	48.58%	(27.51%)	10.38%	(23.70%)	
Q1 – Q3	0.00% – 57.5%		25.00% – 75.00%		0.00% – 4.17%		
Proportion of positive HIV test results among overall number of HIV tests per quarter (*n* = 140)							*p < 0.001*†
Median (IQR)	1.63%	(6.50%)	2.83%	(8.73%)	0.00%	(5.00%)	
Mean (*SD*)	6.47%	(12.41%)	8.02%	(10.16%)	5.16%	(13.96%)	
Q1 – Q3	0.00% – 6.50%		1.27% – 10.00%		0.00% – 5.00%		

Legend: *IQR,* interquartile range; *Q1*, first quartile; *Q3*, third quartile; *SD,* Standard deviation. †From Mann-Whitney U-tests of the null hypothesis that the median value of HIV specialists is equal to that of non-HIV specialists. §From Fisher's Exact tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, by physician group.

Table 15. PrEP Advice during appointments with MSM and transgender persons who met PrEP indication criteria according to the German and Austria PrEP guideline ("at-risk" patients) (20)

Variable	Total Sample		HIV Specialist Status				
			HIV Specialists		Non-HIV Specialists		
Proportion of appointments with "at-risk" MSM and transgender persons in which physicians themselves proactively address the topic of PrEP (*n* = 102)							*p < 0.001*[†]
Median (IQR)	15.48%	(50.0%)	30.00%	(63.50%)	0.00%	(11.32%)	
Mean (SD)	30.20%	(35.34%)	40.70%	(34.21%)	16.36%	(32.21%)	
Q1 – Q3	0.00% - 50.00%		11.50% - 75.00%		0.00% - 11.32%		

Legend: *IQR,* interquartile range; *Q1*, first quartile; *Q3*, third quartile; *SD,* Standard deviation. [†]From Mann-Whitney U-tests of the null hypothesis that the median value of HIV specialists is equal to that of non-HIV specialists.

Self-assessment of PrEP knowledge and advising competencies

Physicians in self-described HIV-specialty practices tended to agree with the competency statements in a statistically significant higher frequency than non-HIV specialists (see ***Table 16***) (20). Correspondingly, the summative knowledge score was much higher for HIV-specialists (*Median* = 20.0, *IQR* = 0.0) than non-HIV specialists (*Median* = 4.0, *IQR* = 11.0), $U = 279.0$, $p < 0.001$ (20).

Table 16. Self-assessment of knowledge and counselling competence (20)

Variable	Total Sample		HIV Specialist Status				
			HIV Specialists		Non-HIV Specialists		
Global assessment: "I am well-informed about PrEP" (*n, %*), *n* = 128							$p < 0.001^{§}$
Strongly disagree	31	(24.2%)	1	(1.8%)	30	(42.3%)	
Disagree	17	(13.3%)	0	(0.0%)	17	(23.9%)	
Neither agree nor disagree	6	(4.7%)	1	(1.8%)	5	(7.0%)	
Agree	16	(12.5%)	4	(7.0%)	12	(16.9%)	
Strongly agree	58	(45.3%)	51	(89.5%)	7	(9.9%)	
Indications: "I am able to comprehensively give patients advice on whether it makes sense to take PrEP in their respective case" (*n, %*), *n* = 128							$p < 0.001^{§}$
Strongly disagree	23	(18.0%)	1	(1.8%)	22	(31.0%)	
Disagree	22	(17.2%)	0	(0.0%)	22	(31.0%)	
Neither agree nor disagree	10	(7.8%)	1	(1.8%)	9	(12.7%)	
Agree	15	(11.7%)	5	(8.8%)	10	(14.1%)	
Strongly agree	58	(45.3%)	50	(87.7%)	8	(11.3%)	
Adverse effects: "I am able to comprehensively give patients advice on the adverse effects of PrEP" (*n, %*), *n* = 128							$p < 0.001^{§}$
Strongly disagree	31	(24.2%)	1	(1.8%)	30	(42.3%)	
Disagree	19	(14.8%)	0	(0.0%)	19	(26.8%)	
Neither agree nor disagree	7	(5.5%)	0	(0.0%)	7	(9.9%)	
Agree	11	(8.6%)	3	(5.3%)	8	(11.3%)	
Strongly agree	60	(46.9%)	53	(93.0%)	7	(9.9%)	
Modalities of intake: "I am able to comprehensively give patients advice on the possible modalities of intake of PrEP (e.g., continuous vs. on-demand)" (*n, %*), *n* = 128							$p < 0.001^{§}$
Strongly disagree	31	(24.2%)	1	(1.8%)	30	(42.3%)	
Disagree	20	(15.6%)	0	(0.0%)	20	(28.2%)	
Neither agree nor disagree	5	(3.9%)	1	(1.8%)	4	(5.6%)	
Agree	10	(7.8%)	2	(3.5%)	8	(11.3%)	
Strongly agree	62	(48.4%)	53	(93.0%)	9	(12.7%)	
Investigations: "I am able to comprehensively give patients advice on the medical investigations necessary during the use of PrEP" (*n, %*), *n* = 128							$p < 0.001^{§}$
Strongly disagree	29	(22.7%)	1	(1.8%)	28	(39.4%)	
Disagree	20	(15.6%)	0	(0.0%)	20	(28.2%)	
Neither agree nor disagree	6	(4.7%)	1	(1.8%)	5	(7.0%)	
Agree	9	(7.0%)	2	(3.5%)	7	(9.9%)	
Strongly agree	64	(50.0%)	53	(93.0%)	11	(15.5%)	
Knowledge score (0-20), *n* = 128							$p < 0.001^{†}$
Median (*IQR*)	15.0	(17.0)	20.0	(0.0)	4.0	(11.0)	
Mean (*SD*)	11.89	(8.43)	19.23	(2.96)	6.49	(6.76)	
Q1 – Q3	3.0-20.0		20.0-20.0		0.0-11.0		

Legend: *IQR*, interquartile range; *Q1*, first quartile; *Q3*, third quartile; *SD*, Standard deviation. §From Fisher's Exact tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each

category, by physician group. †From Mann-Whitney U-tests of the null hypothesis that the median value of HIV-specialists is equal to that of non-HIV-specialists.

Attitudes towards PrEP

Physicians working in HIV-specialty practices agreed with all positive statements and disagreed with the negative statement about PrEP far more frequently than physicians working in non-HIV-specialty practices (see ***Table 17***) (20). Mirroring the summative knowledge score, HIV-specialists had an overall higher attitude score and correspondingly more positive opinion of PrEP (*Median* = 18.0, *IQR* = 3.0) than non-HIV-specialists (*Median* = 13.0, *IQR* = 5.25) $U = 588$, $p < 0.001$ (20).

Table 17. Attitudes towards PrEP (20)

Variable	Total Sample		HIV Specialist Status				
			HIV Specialists		Non-HIV Specialists		
Global assessment: "I think that PrEP is an important element of HIV prevention strategies" (*n, %*), *n* = 126							$p < 0.001^{\S}$
Strongly disagree	1	(0.8%)	0	(0.0%)	1	(1.4%)	
Disagree	7	(5.6%)	1	(1.8%)	6	(8.7%)	
Neither agree nor disagree	10	(7.9%)	1	(1.8%)	9	(13.0%)	
Agree	30	(23.8%)	4	(7.0%)	26	(37.7%)	
Strongly agree	78	(61.9%)	51	(89.5%)	27	(39.1%)	
Reliability: "I think that PrEP is a reliable method to protect oneself from HIV" (*n, %*), *n* = 124							$p < 0.001^{\S}$
Strongly disagree	5	(4.0%)	0	(0.0%)	5	(7.5%)	
Disagree	8	(6.5%)	0	(0.0%)	8	(11.9%)	
Neither agree nor disagree	19	(15.3%)	4	(7.0%)	15	(22.4%)	
Agree	44	(35.5%)	16	(28.1%)	28	(41.8%)	
Strongly agree	48	(38.7%)	37	(64.9%)	11	(16.4%)	
Adverse effects: "I think that PrEP is a method to protect oneself from HIV that has few side effects" (n, %), n = 124							$p < 0.001^{\S}$
Strongly disagree	5	(4.0%)	0	(0.0%)	5	(7.4%)	
Disagree	19	(15.3%)	2	(3.6%)	17	(25.0%)	
Neither agree nor disagree	36	(29.0%)	11	(19.6%)	25	(36.8%)	
Agree	37	(29.8%)	21	(37.5%)	16	(23.5%)	
Strongly agree	27	(21.8%)	22	(39.3%)	5	(7.4%)	
Availability of better alternatives: "I think that PrEP is unnecessary, because there are better alternatives to protect oneself from HIV" (*n, %*), *n* = 121							$p = 0.003^{\S}$
Strongly disagree	54	(44.6%)	34	(59.6%)	20	(31.3%)	
Disagree	38	(31.4%)	17	(29.8%)	21	(32.8%)	
Neither agree nor disagree	23	(19.0%)	5	(8.8%)	18	(28.1%)	
Agree	3	(2.5%)	1	(1.8%)	2	(3.1%)	
Strongly agree	3	(2.5%)	0	(0.0%)	3	(4.7%)	
Reimbursement of costs: "I think that PrEP should be paid for by the statutory health insurance" (*n, %*), *n* = 124							$p = 0.001^{\S}$
Strongly disagree	10	(8.1%)	1	(1.8%)	9	(13.4%)	
Disagree	15	(12.1%)	3	(5.3%)	12	(17.9%)	
Neither agree nor disagree	23	(18.5%)	10	(17.5%)	13	(19.4%)	
Agree	25	(20.2%)	9	(15.8%)	16	(23.9%)	
Strongly agree	51	(41.1%)	34	(59.6%)	17	(25.4%)	
Attitude score (0-20), *n* = 112							$p < 0.001^{\dagger}$
Mdn (IQR)	15.5	(5.0)	18.0	(3.0)	13.0	(5.25)	
M (SD)	14.93	(3.92)	17.29	(2.59)	12.90	(3.78)	
Min; Max	13.0 – 18.0		16.0 – 19.0		10.0 – 15.25		

Legend: *IQR*, interquartile range; *Q1*, first quartile; *Q3*, third quartile; *SD*, Standard deviation. †From Mann-Whitney U-tests of the null hypothesis that the median value of HIV-specialists is equal to that of non-HIV-specialists §From Fisher's Exact tests of the null hypothesis stating that there is no statistically significant difference between the observed and expected frequencies in each category, according to physician group.

Identification of and active advisement history of guideline-determined "at-risk" patients

Physicians were given a list of patients with differing risk profiles and were asked how likely they would actively speak to the listed patients about PrEP (see ***Table 18***). According to the German and Austrian guidelines, the following HIV-negative patients are deemed to have higher-risk profiles for HIV:

Table 18. German- and Austria guideline-defined HIV-negative persons at substantial risk for infection with HIV (23)

HIV-negative people who:
…report having anal sex without condoms within the last 3-6 months and/or are planning to do so within the coming months or who have had an STI in the last 12 months
…live in a serodiscordant constellation with a viral HIV-positive partner not taking ART, not fully virally suppressed under ART or who has just begun ART (essentially having HIV-RNA viral load that isn't suppressed under <200 RNA-Copies/mL)
…have sex without condoms with partners who could likely have an undiagnosed HIV infection
…IV-drug using persons who use unsterile needles

Physicians in both groups responded with a wide variety of responses to all proposed patients. There was no clear response direction among either group. All responses were found to be statistically significant aside from responses regarding patients who are receiving a diagnosis of a non-bacterial STI (e.g., herpes genitalis, condylomata acuminata). The guideline-defined groups with an indication for PrEP are highlighted above. Detailed below in ***Table 19*** are the likelihoods of each specialty group actively advising a patient with that risk profile to take PrEP. Both groups show a wide spread of responses; however statistically significant differences emerged among (1) non-monogamous CAI, (2) sex with random partners, (3) having a history of PEP use, (4) having a history of "chemsex" or (5) living in a serodiscordant relationship.

Table 19. Self-reported likelihood of active advisement according to patient risk profile

"How likely would you actively advise an HIV-negative MSM or Transgender patient who…"

Variable	Total Sample		HIV Specialist Status				
			HIV Specialists		Non-HIV Specialists		
…indicates that they have condomless anal sex outside of a monogamous relationship (*n, %*), *n* = 134							$p < 0.001^{§}$
Definitely not	5	(3.7%)	0	(0.0%)	5	(6.8%)	
Probably not	7	(5.2%)	0	(0.0%)	7	(9.5%)	
Unsure	9	(6.7%)	0	(0.0%)	9	(12.2%)	
Probably yes	44	(32.8%)	18	(30.0%)	26	(35.1%)	
Absolutely	69	(51.5%)	42	(70.0%)	27	(36.5%)	
…indicates that they have sex with random partners (*n, %*), *n* = 132							$p < 0.001^{§}$
Definitely not	31	(23.5%)	20	(33.3%)	11	(15.3%)	
Probably not	7	(5.3%)	0	(0.0%)	7	(9.7%)	
Unsure	17	(12.9%)	2	(3.3%)	15	(20.8%)	
Probably yes	46	(34.8%)	25	(41.7%)	21	(29.2%)	
Absolutely	31	(23.5%)	13	(21.7%)	18	(25.0%)	
…is receiving a diagnosis of a bacterial STI for the first time (e.g., Syphilis, gonorrhea, chlamydia) (*n, %*), *n* = 134							$p = 0.003^{§}$
Definitely not	34	(25.4%)	24	(40.0%)	10	(13.5%)	
Probably not	7	(5.2%)	1	(1.7%)	6	(8.1%)	
Unsure	11	(8.2%)	2	(3.3%)	9	(12.2%)	
Probably yes	42	(31.3%)	18	(30.0%)	24	(32.4%)	
Absolutely	40	(29.9%)	15	(25.0%)	25	(33.8%)	
…is receiving a diagnosis of a bacterial STI for the second or more time (e.g. Syphilis, gonorrhea, chlamydia) (*n, %*), *n* = 132							$p = 0.003^{§}$
Definitely not	44	(33.3%)	29	(49.2%)	15	(20.5%)	
Probably not	3	(2.3%)	0	(0.0%)	3	(4.1%)	
Unsure	8	(6.10%)	1	(1.7%)	7	(9.6%)	
Probably yes	23	(17.4%)	8	(13.6%)	15	(20.5%)	
Absolutely	54	(40.9%)	21	(35.6%)	33	(45.2%)	
…is receiving a diagnosis of a non-bacterial STI (e.g., herpes genitalis, condylomata acuminata) (*n, %*), *n* = 134							$p = 0.037^{§}$
Definitely not	26	(19.4%)	16	(27.1%)	10	(13.3%)	
Probably not	8	(6.0%)	1	(1.7%)	7	(9.3%)	
Unsure	16	(11.9%)	5	(8.5%)	11	(14.7%)	
Probably yes	53	(39.6%)	27	(45.8%)	26	(34.7%)	
Absolutely	31	(23.1%)	10	(16.9%)	21	(28.0%)	
…reports having taken or reports current use of HIV-Post exposition prophylaxis (PEP) or has received a prescription for PEP from you (*n, %*), *n* = 134							$p < 0.001^{§}$
Definitely not	45	(33.6%)	31	(51.7%)	14	(18.9%)	
Probably not	5	(3.7%)	1	(1.7%)	4	(5.4%)	
Unsure	11	(8.2%)	2	(3.3%)	9	(12.2%)	
Probably yes	31	(23.1%)	7	(11.7%)	24	(32.4%)	
Absolutely	42	(31.3%)	19	(31.7%)	23	(31.1%)	
…reports having sex under the influence of drugs ("chemsex") (*n, %*), *n* = 135							$p < 0.001^{§}$
Definitely not	42	(31.1%)	29	(48.3%)	13	(17.3%)	
Probably not	6	(4.4%)	0	(0.0%)	6	(8.0%)	
Unsure	7	(5.2%)	0	(0.0%)	7	(9.3%)	
Probably yes	35	(25.9%)	11	(18.3%)	24	(32.0%)	
Absolutely	45	(33.3%)	20	(33.3%)	25	(33.3%)	
…reports living in a relationship with an HIV-positive partner whose viral load is not currently suppressed* (*n, %*), *n* = 135							$p < 0.001^{§}$
Definitely not	48	(35.6%)	34	(56.7%)	14	(18.7%)	
Probably not	3	(2.2%)	0	(0.0%)	3	(4.0%)	
Unsure	7	(5.2%)	0	(0.0%)	7	(9.3%)	
Probably yes	22	(16.3%)	5	(8.3%)	17	(22.7%)	
Absolutely	55	(40.7%)	21	(35.0%)	34	(45.3%)	

Legend: §From Pearson's Chi-squared tests of the null hypothesis stating that there is no statistically significant difference between the observed and expected frequencies in each category, according to specialist type. *A guideline-determined indication for PrEP

Multiple linear regression of the proportion of proactive PrEP advice

A multiple linear regression was developed to determine predictive factors associated with proportion of proactive PrEP advice give n by physicians to "at-risk" patients (20). We applied both a backwards-elimination method and a stepwise forward elimination

method (both included a stopping rule of $p<0.2$ for the exclusion or inclusion of each variable) (20). The same equation was found using both methods ($F(3,79) = 7.70$, $p<0.001$, $n=83$), with $R^2 = 0.165$ (see ***Table 20***) (20). This indicates that, for each jump in location size, the proactive PrEP advisement increased by 6.11%, and for each point increase in knowledge or attitude score, proactive PrEP advisement increased by 1.78% and 1.85%, respectively.

Table 20. Multiple linear regression to predict the proportion of PrEP advice provided proactively to MSM and trans persons who meet the criteria to be offered PrEP according to the German and Austrian guideline ("at-risk" patients) (20)

Predictors	**Coefficient (Robust SE)**		**Beta**	***p***	**VIF**
Constant	-32.632	(16.238)		0.048	
Size of the city [1]	6.107	(4.553)	0.170	0.184	1.39
Knowledge score[2]	1.782	(0.585)	0.320	0.003	2.00
Attitudes score[3]	1.851	(1.031)	0.191	0.077	1.57

Legend: *SE*, standard error; *VIF*, variance inflation factor; [1] Size of the city coded in 4 categories with 0 indicating more than 1,000,000 inhabitants and 3 indicating less than 10,000 inhabitants [2] Scale from 0 to 20 points, with higher scores indicating a more positive self-assessment of knowledge about PrEP and counselling competence; [2] Scale from 0 to 20 points, with higher scores indicating a more positive attitude towards PrEP.

Physicians' perceived barriers to PrEP initiation

121 respondents participated in rating a list of barriers according to their perceived relevance towards patients initiating PrEP (20). The most relevant barriers were as follows: patients underestimating their own risk of acquiring an HIV infection (*Median* = 8.00, *IQR* = 4.0), difficulties in finding a doctor to prescribe PrEP (*Median* = 8.0, *IQR* = 5.5), and the time required for regular visits to the doctor (*Median* = 7.0, *IQR* = 6.0) (20). Respondents also indicated that the time-consuming management of PrEP patients (*Median* = 7.0, *IQR* = 4.0) was a relevant barrier for physicians (20). The data are presented in ***Table 21***.

Table 21. Barriers to initiate PrEP as perceived by participating physicians (20)

Barrier	n	*Median*	(IQR)
Patient-associated Barriers			
Assessment of the own risk of getting infected with HIV as too low to take PrEP	69	8.0	(4.0)
Difficulties finding a doctor who prescribes PrEP	74	8.0	(5.5)
Time required for regular visits to the doctor	66	6.0	(6.0)
The monthly costs of the PrEP medication	69	6.0	(6.0)
Lack of information about PrEP in patient-friendly language	68	5.0	(5.0)
Lack of information about PrEP in the native language of the client	68	5.0	(5.0)
Worries about getting infected with other STIs	71	5.0	(5.0)
Cultural barriers	72	5.0	(6.0)
The costs of the laboratory tests	73	5.0	(6.0)
Worries about severe or permanent side effects	68	4.0	(5.0)
Worries about mild or temporary side effects	67	3.0	(4.0)
Worries about stigmatization in the peer group	69	3.0	(5.0)
Physician-associated Barriers			
For doctors, the management of PrEP-Patients is too time-consuming	69	7.0	(4.0)
It is difficult for doctors to identify patients who would benefit from PrEP	75	3.0	(6.0)

Legend: *IQR*, interquartile range

Educational Materials

The 121 respondents answered questions regarding educational materials and tools that could help increase PrEP prescriptions and/or enable higher quality PrEP counselling (see ***Table 22***) (20). Patient decision aids presenting information in patient-friendly language (*n* = 87, 71.9%) and in different languages (*n* = 68, 56.2%) were chosen most frequently among respondents (20). Nearly half of respondents (*n* = 65, 53.7%) indicated that a national guideline with clearly stated indications, contraindications and necessary bloodwork would be helpful (20). Furthermore, slightly over half of respondents (*n* = 65, 53.7%) responded that educational materials and/or training in the management of PrEP would be helpful (20).

Significantly more non-HIV-specialists indicated that they would like to receive educational materials and/or training regarding the management of PrEP users (61.9% vs. 43.6%, $\chi^2(df = 1, n = 118) = 3.938$, $p = 0.047$) and regarding identifying patients who would benefit from taking PrEP (50.8% vs. 25.5%, $\chi^2(df = 1, n = 118) = 7.926$, $p = 0.005$).

Table 22. Interest in educational materials for HIV PrEP

Variable	Total Sample		HIV Specialist Status				
			HIV Specialists		Non-HIV Specialists		
A guideline with clearly stated indications, contraindications and necessary bloodwork (*n, %*), *n* = 118							$p = 0.004^{\dagger}$
Yes, would be helpful	64	(45.8)	22	(40.0)	42	(66.7)	
No, would not be helpful	54	(54.2)	33	(60.0)	21	(33.3)	
A decision-aid for patients in patient-friendly language (*n, %*), *n* = 118							$p = 0.875^{\dagger}$
Yes, would be helpful	85	(72.0)	40	(72.7)	45	(71.4)	
No, would not be helpful	33	(38.0)	15	(27.3)	18	(28.6)	
A decision-aid for patients in different languages (*n, %*), *n* = 118							$p = 0.004^{\dagger}$
Yes, would be helpful	67	(56.8	39	(29.1)	28	(44.4)	
No, would not be helpful	51	(43.2)	16	(70.9)	35	(55.6)	
An App- or SMS-based reminder service to increase PrEP adherence (*n, %*), *n* = 118							$p = 0.006^{\dagger}$
Yes, would be helpful	55	(46.6)	33	(60.0)	22	(34.9)	
No, would not be helpful	63	(53.4)	22	(40.0)	41	(65.1)	
Information or training for doctors to identify patients who could benefit from PrEP (*n, %*), *n* = 118							$p = 0.005^{\dagger}$
Yes, would be helpful	46	(39.0)	14	(25.5)	32	(50.8)	
No, would not be helpful	72	(61.0)	41	(74.5)	31	(49.2)	
Information or training for doctors in the prescription and management of PrEP (*n, %*), *n* = 118							$p = 0.047^{\dagger}$
Yes, would be helpful	63	(53.4)	24	(43.6)	39	(61.9)	
No, would not be helpful	55	(46.6)	31	(56.4)	24	(38.1)	
Information or training for doctors around the topic "Speaking with Patients about Sexuality" (*n, %*), *n* = 118							$p = 0.278^{\dagger}$
Yes, would be helpful	35	(29.7)	19	(34.5)	16	(25.4)	
No, would not be helpful	83	(70.3)	36	(65.5)	47	(74.6)	
None (*n, %*), *n* = 118							$p = 0.060^{\dagger}$
Yes, would be helpful	3	(2.5)	3	(5.5)	25	(30.0)	
No, would not be helpful	115	(97.5)	52	(94.5)	35	(46.1)	

Legend: †From Pearson's Chi-squared tests of the null hypothesis stating that there is no statistically significant difference between the observed and expected frequencies in each category, according to specialist type.

Data sourced partially from Sammons, Mary Katherine, et. al.. (20) Copyright 2021 Sammons, Gaskins, Kutscha, Nast and Werner.

6. Discussion

When seeking to evaluate the success of a prophylactic treatment, all ecological domains must be evaluated. The first publication sought to understand the patient's perspective (18). We saw that there was a relatively high level of awareness amongst respondents (90%); however, roughly half of all respondents still felt poorly informed

about PrEP even despite two thirds of them currently taking or having previously taken chemoprophylaxis (18). When we couple this with the high frequency of informal sourcing (e.g., imports, pills from a PEP prescription, using a friend's HIV medication), this points to a weakness from the providers' and/or counsellors' sides to ensure patients start and continue properly taking PrEP (18). When patients informally source their medication, physicians will not be able to review side effects and test for other STIs, leading to delays in side effect recognition and STI diagnoses. Furthermore, it is well-documented that improper PrEP usage can lead to incomplete suppression of the virus and cause drug selective pressure, leading to drug resistance (24-27). Another study among German PrEP users in 2018 showed that informal PrEP users were more likely to start PrEP without baseline chemoprophylaxis testing (i.e. HIV status, kidney retention parameters, etc.), and neglecting to test during PrEP use was also associated with informal usage (28). Failure to test before and/or during PrEP use puts patients at risk of contracting a resistant strain of HIV. With frequent monitoring via trained physicians, early detection and viral suppression is possible, reducing both the likelihood of disease progression and/or population spread.

There are few direct studies involving individuals sourcing PrEP informally (i.e. "DIY PrEP", "wild PrEP", "informal sourcing" or "informal PrEP use" – typically sourced through websites, via friends' medication or other non-prescription sources)(29). The most recent data in Germany suggest a lack of baseline and/or follow-up testing among such users, as well as more on-demand use among them which may be more confusing for many to determine the adequate dosing without professional supervision (28-30). In a qualitative study among informal PrEP users in England, some respondents reported switching to daily dosing after finding DIY on-demand dosing to be confusing and expensive (30). The patients in our questionnaire were participants sourced from NG centers and HIV specialty practices in Berlin (18). This may have led to a selection bias towards patients whose physician contacts would most likely be HIV specialists themselves, either through referrals from the counsellors or via the patient cohort in the selected physician practices. In our counsellors' study, we saw that counsellors from such testing centers more likely had SOPs for PrEP and had both greater knowledge and attitude scores compared to LHOs (see ***Tables 9*** and ***10***) (19); our physicians' study also showed that HIV-specialists had higher self-reported knowledge (higher knowledge scores) than non-specialists (see ***Table 15***) (20). Our

HIV-specialists also had higher rates of PrEP prescription to at-risk patients with 50% of all at-risk patients seen receiving a PrEP prescription compared to non-HIV specialists (0.00%) (see ***Table 13***) (20). When patients from well-informed sources are able to be counselled effectively and monitored safely, PrEP adherence can be maintained in order to reduce the likelihood of resistance and breakthrough infections. Follow-up studies regarding adherence and breakthrough infections among all PrEP prescribers (not just HIV specialists) are needed to best determine adherence aids and barriers.

The PrEP care continuum (see ***Figure 1***) ends with consistent follow-up to ensure proper PrEP intake, maintained HIV negative serostatus and/or HIV treatment initiation in the case of seroconversion. For many patients, their initial contact is at a counsellor's office, at their local health department or part of a routine STI assessment at a non-HIV-specialist physician's office.

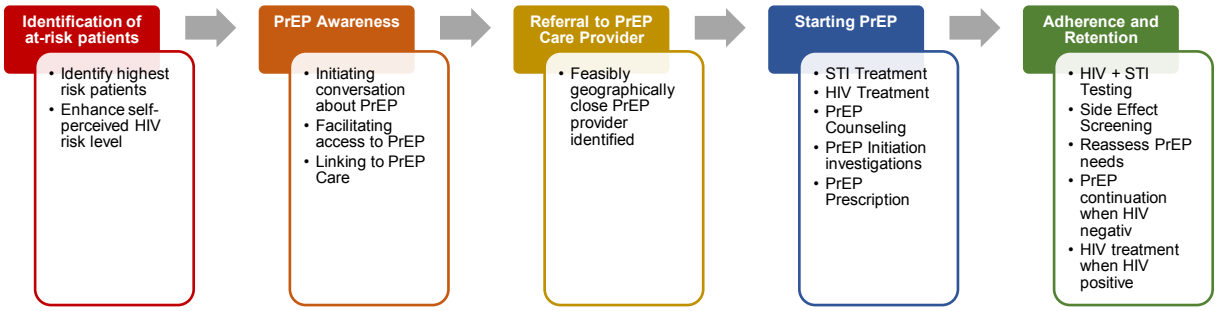

Figure 1. PrEP Care Continuum

Figure based on text from Nunn, et al. (1)

By providing proper training for counsellors, the PrEP continuum can help move at-risk patients towards initiation and retention by ensuring a referral to a physician's practice is made. Interestingly, German LHOs (Gesundheitsämter) have a wider range of important functions in their communities with the treatment and prevention of STIs and HIV being but one component, and the contact persons for sexual health queries can range from psychologists, nurses, social workers or even physicians. Our study indicated a discrepancy between these two groups, showing NG counsellors to have greater self-described knowledge of PrEP than their government counterparts, despite LHOs running more HIV tests and having more positive HIV tests per month than NG counselling centers (19). The studies performed did not inquire as to whether a referral was made to a physician's office or whether the on-staff physician at the LHOs would

be directly involved if clients wanted to start PrEP. While active advisement does help increase patient knowledge, it does not necessarily move patients who could benefit from PrEP further along the care continuum. Follow-up studies would be helpful to assess whether and how counsellors are connecting patients to providers and maintaining an active care continuum.

For counsellors and LHOs in large cities, referring patients to knowledgeable physicians to start and maintain PrEP can be onerous depending on their location. One of the most frequently cited barriers to starting chemoprophylaxis in our studies was “difficulties in finding a doctor who prescribes PrEP” (18-20). Our physicians’ study showed that the majority of our HIV specialists were located in more populous areas (cities with 100,000 inhabitants or more) with nearly 50% located in metropolises with 1 million or more inhabitants; however, over half of our non-HIV-specialists reported working in cities with a population of less than 100,000 (20). Given the current PrEP-licensure program[1] requires in-person internships with HIV-specialists, many non-HIV-specialists would have to temporarily close their practice and travel for at least two days of in-person training, something that has become increasingly difficult given the current pandemic-related travel restrictions that began shortly after PrEP coverage started in Germany. With hurdles to PrEP-licensure for physician come hurdles for patients who could benefit from PrEP, especially in areas without HIV specialists. Even if physicians who are not licensed to bill for PrEP services want to refer patients to colleagues who can, this pushes the geographical burden onto patients who may be even less equipped to travel for regular appointments and prescriptions.

While the Sars-CoV-2 pandemic may have created barriers for travel, the pandemic has allowed for creative solutions for in-person communication with more widespread use of improved online training modules and modern televisits with doctors. To help reduce the travel burden for trainees, introducing online training modules for PrEP licensure and offering partnered televisits with HIV specialists could greatly help decrease the strain on non-HIV-specialists seeking licensure. When more physicians

[1] Currently, PrEP licensure is only available after a 16-hour internship at either an inpatient or outpatient HIV care facility where trainees are required to either performed supervised consultations or to have witnessed consultations of 15 patients either living with HIV/AIDS or considering taking PrEP. Additionally, 8 Continuing Medical Education (CME) points are to be obtained within a year of requesting licensure [31. Vereinbarung über die HIV-Präexpositionsprophylaxe zur Prävention einer HIV-Infektion gemäß § 20j SGB V, (2019).

are able to identify patients, begin PrEP treatment and ensure adherence, patient can feel safer and more confident in how they choose to protect themselves.

The most commonly cited barrier to PrEP initiation among physicians was patients' self-assessed risk of becoming infected with HIV being too low to start chemoprophylaxis, and both our counsellors and physicians cited a lack of patient-friendly information in their native languages as relevant barriers to starting PrEP (19, 20). Together, this points to an information gap that cannot be solved by well-trained physicians and counsellors alone. When all groups of care providers (counsellors and physicians) were asked what information aids would help improve PrEP uptake, the most requested were patient-or client-centered (flyers in patient-appropriate language or multiple languages) (19, 20). Having fact-based information readily available for patients to review outside of the office helps ensure the flow of reliable information in often time-starved environments in most offices and practices. Studies show the relevance of paper-based informational leaflets (32, 33); however, good design is necessary to avoid confusion or choice anxiety so as to increase patient eagerness to read them (34). Furthermore, given that most of our respondents informed themselves via friends/acquaintances, magazines/journals/blogs and dating apps/platforms before physicians and lastly counsellors, it is important to ensure information dissemination through means that patients actively use (18). Misinformation about health topics has been a widely-discussed issue, and HIV PrEP is no exception (35-39). Making data easy to find online via popular blogs and magazines or partnering with dating apps to post informative ads could help guarantee that patients have access to reliable information from sources they are currently using.

While sharing patient-centered information via leaflets or posts does help increase awareness, it does not replace the due diligence of targeted, active advisement. Both of our provider-centered studies showed that providers who are better-informed are more likely to actively advise at-risk individuals. Issuing training in identifying patients, initiating and monitoring PrEP supports providers to make certain that at-risk individuals understand their risk and how PrEP can help mitigate it. Part of adequate training includes having an easy-to-access national guideline, streamlined PrEP training programs for prescribers and putting evidence-based SOPs in advising facilities.

The German and Austrian national guideline for HIV PrEP states that those with "substantial risk" for becoming infected with HIV should be recommended PrEP[2](23). The guideline further states that Germany, as a whole, is a low-risk country; however, for certain groups, the risk could be much higher (23). The groups for whom the guideline explicitly recommends PrEP have been listed previously in this dissertation (see ***Table 17***); yet, in the guideline's clarifying text, they state that individual cases may lead to increased risk when sex is performed without a condom or when patients directly ask for PrEP (23). The diagnosis of an STI (whether bacterial or non-bacterial) was not listed as an indication for PrEP or an indication to advise for PrEP.

We sought to assess respondents' awareness of the current German indications for PrEP initiation by providing a list of scenarios and asking how likely providers would actively advise the hypothesized patient to take PrEP (20). The scenarios were based on the German-Austrian guideline-defined patient groups which were listed in the question section prior; many of the scenarios were directly guideline-defined, but the majority were near-indications (i.e., by themselves were not direct indications, but when in context of CAI, would be risk-increasing) (20). Responses from the participants were varied, and there was a statistically significant difference between HIV specialists and non-HIV specialists (20). Even among our well-informed group of STI-specialists there were often response discrepancies with no clear response direction (see ***Table 21***) (20).

The guidelines themselves state that PrEP would be indicated in a much wider array of settings than most other countries' guidelines (23). The guideline states that there is a high level of accurate self-assessment among potential PrEP patients, allowing a careful risk evaluation to be performed. Interestingly, our respondents cited patients' inaccurate self-assessed risk level to be the greatest barrier to PrEP initiation (23). Furthermore, multiple studies have concurred that patients are less likely to report embarrassing, community-defined "shameful" or clinician-disapproved behavior to providers (40-43). When physicians across the HIV-knowledge spectrum state that patients are often not reliable risk-assessors, it is important to provide clear indication criteria that are not primarily dependent upon patient-reported data (i.e. condomless

[2] German: „Die orale HIV Präexpositionsprophylaxe soll als prophylaktische Maßnahme Menschen mit substanziellem HIV-Infektionsrisiko angeboten werden." English: „The oral HIV pre-exposure prophylaxis should be offered as a prophylactic method to people with a substantial HIV infection risk."

anal sex), especially given the well-documented medical stigma and healthcare discrimination against LGBTQIA+ patients (44-46).

When we consider guidelines outside of Germany, we see there is much room for improvement. The guidelines for PrEP from the United Kingdom provide a solid basis for providers who may have little experience in performing risk-assessments for PrEP by outlining statements that may indicate a patients' increased risk of contracting HIV without having to target patients with potentially stigmatizing language (47). The current Centers for Disease Control (CDC) guideline in the United States goes much further by recommending that all sexually active adults and adolescents should be informed of PrEP to prevent HIV infection because of the stigma surrounding most patients who reveal higher-risk sexual activities (48). The previous 2017 CDC guidelines recommended PrEP for MSM only after either anal sex without condoms or the diagnosis of a bacterial STI within the past 6 months was found (49). Uganda's current HIV PrEP guidelines include the use of PEP, sex workers and inconsistent condom usage without specifying birth or identifying genders (50). By incorporating other countries' less "obvious" risk-assessment aids for providers, widening indication criteria and incorporating more inclusive guideline language, physicians and counsellors will be able to identify patients more easily with fewer stigmatizing interactions (i.e. not forcing a patient to fill out sexual health questionnaires or sexual health interrogations) (51). By decreasing stigmatization from providers or counsellors, patient trust can be built and adherence increased (52-54).

All the studies mentioned in this paper were performed between 2017 and 2019, with the physicians' study ending collection a month after PrEP coverage by the statutory health insurance system was announced.

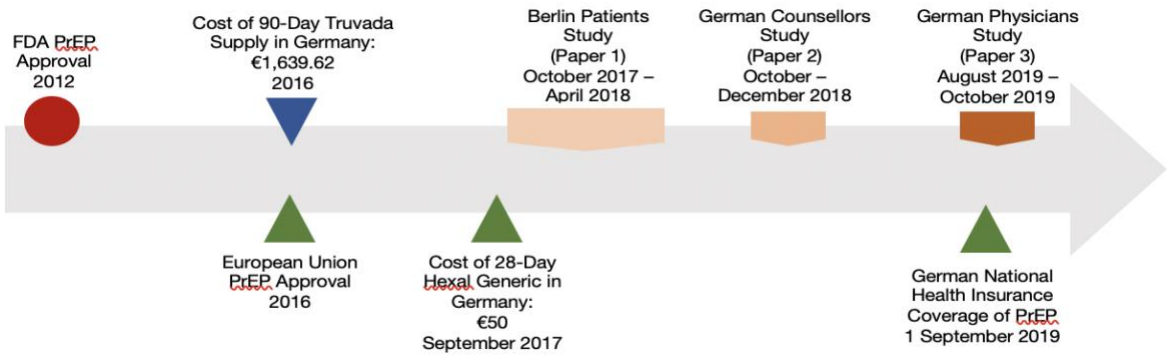

Figure 2. Timeline of HIV PrEP Events and Data Collection[3]

There have not yet been any follow-up questionnaires since the ending of the third study; however, new types of chemoprophylaxis and new methods of chemoprophylaxis have been introduced with long-acting intramuscular injections of cabotegravir receiving FDA approval in December 2021 (56). The AIDS Vaccine Advocacy Coalition's regularly updated infographic on the HIV PrEP pipeline shows the current state of HIV PrEP research with a plethora of new antiretrovirals in a variety of formulations from long acting injectables, implants, oral pills, vaginal rings and vaginal gels (57). With the array of prevention methods on the horizon, increased sexual safety, enhanced quality of life and decreased HIV burden will follow if political bodies, PrEP care providers and patients are ready.

7. Limitations

The aforementioned studies focused strongly on the LGBTQIA+ community, as they, specifically the MSM community, carry the largest disease burden in Germany. Currently, the statutory health system allows for internists, dermatologists, urologists, and also pediatricians and gynecologists to receive the designation to prescribe PrEP. The studies published reflect only part of these physicians' patient groups, namely those who are 18+, MSM or are transgender women. PrEP may be prescribed to those who are aged 16 and up; yet this age group was not assessed in any of these studies.

[3] When PrEP was first introduced in Germany without available generics. The cost of Truvada at that time was ca. 560€ per month or €1639.62 for a 90-day supply. In 2017, two generic versions from Ratiopharm and Hexal were introduced, sinking the costs to €50 or 69,90€ for a 30-day supply55.
Borsch J. Konstengünstige PrEP? Da gibt es jetzt auch was von ratiopharm. DAZonline [Internet]. 2017 15 May 2018. Available from: https://www.deutsche-apotheker-zeitung.de/news/artikel/2017/11/30/kostenguenstige-prep-da-gibt-es-jetzt-auch-was-von-ratiopharm..

Young MSM have specific needs, face different barriers and live with different stigmas than adult MSM. Furthermore, heterosexual, cisgendered female sex workers or heterosexual, cisgendered females living in relationships with at-risk sexual partners were not included in this study. Both gynecologists and pediatricians were not included in the physicians' study both due primarily to our exclusion of their primary patient groups. To fully assess PrEP implementation, all patient cohorts should have been assessed by our studies.

Unlike in many English-speaking countries, Germany does not have traditional "GUM" (genitourinary medicine) clinics that are not primarily focused on MSM, gay and/or transgender female clients. Whether the HIV PrEP care continuum can apply to heterosexual, cisgendered females or heterosexual, cisgendered males who may not directly seek out German counselling centers or local health departments remains unclear. To date, there is very little research regarding HIV among cisgender, heterosexual female sex workers, teenage sex workers or teenage MSM within Germany. Furthermore, scant research is available concerning HIV PrEP implementation among IV-drug users in Germany. The Robert Koch Institute has seen a decrease in new infections among MSM in Germany; however, there have been small but steady increases in new infections among IV-drug users and among heterosexuals. Additional research among these groups is necessary to better understand how to ensure they are properly protected. The American strategy of active advisement among all sexually active adults would help decrease the stigma of PrEP by opening the door to a wider conversation on sexual health while ensuring anyone who might need it would have access.

Additional limitations of these studies include the time at which they were conducted. The studies were performed at different times, making it difficult to truly coordinate responses between the providers, counsellors and patients. The patients' study was performed at PrEP's genesis in Germany: the stark price reduction happened during our study, and the topic was just starting to grow in the media at large (18). Our providers' and counsellors' studies were performed at least two years later (in total 3 years after the EU approval of PrEP) (19, 20). There was a relatively high awareness of PrEP among all respondents which would seemingly contradict our patients' experiences with ill-prepared providers; however, the time between our patients and providers'/ counsellors' studies provided ample time for increased media attention,

guideline development, PrEP coverage by the health insurance systems and a requirement plan for accreditation for PrEP services allowing for cost coverage by statutory health insurances. There has not been any follow-up study performed to assess whether patients are able to access more trustworthy information sources, have improved access to HIV PrEP providers or better understanding of PrEP and its side effects.

Additionally, follow-up studies regarding physician or counsellor experiences after the PrEP roll-out have not been performed. This would help provide insight into whether the new coverage of PrEP has impacted physicians' scheduling capabilities. Many physicians cited that PrEP management would be too time consuming to offer patients; however, we have not assessed whether that is the case with non-HIV-specialists who would be offering this service with the new PrEP billing capabilities. Given that our providers cited this as the top physician barrier to offering PrEP, this would be important to help assuage fears of PrEP's impact.

Another important limitation was seen in our counsellors' study. When we are seeking to assess whether PrEP is, indeed, reaching those who need it most, we should have examined whether those along the PrEP continuum are ensuring patients continue to PrEP initiation and maintenance. Our counsellors were not asked whether they actively refer to physicians who can prescribe PrEP. While ensuring they actively advise clients is important for informing patients, it does not ask whether the full role of PrEP counselling is being filled. Patients may not understand how to find a physician or where knowledgeable practices are located; by making active referrals, clients aren't lost in the counselling to prescribing black box.

Equally important was the follow-up among physicians who actively advised their patients. If the continuum is to achieve maintenance and ensure HIV negative patients remain negative, questions regarding the estimated percentage of PrEP patients who make follow-up appointments for testing and re-prescriptions should have been included in our physicians' study.

The use of non-validated study instruments in both our counsellors' and physicians' studies are important limitations. There are currently no similarly validated questionnaires in German to assess counsellor or physician knowledge and experiences; nonetheless, our scores produced may, therefore, not be fully

representative of our respondents' knowledge or attitudes towards PrEP. Furthermore, as the knowledge statements were self-assessed, respondents' true knowledge may differ largely than that which is reported here, and the advising capabilities of our respondents may not be directly related to the score which we calculated in these papers.

Our physicians' study had a very low response rate of 5.53% (20) . As such low response rates have been common in many other studies involving office-based health practitioners, we undertook many additional steps to encourage active participation in our study (58). Despite sending follow-up emails, posting QR codes to our online survey at a well-attended national STI conference and even submitting the survey to the email listings of the German AIDS Association and the German STI Association, the response rate remained very low (20), making it difficult to clearly extrapolate our data across the entire population of both HIV specialists and non-specialists in Germany. The low response rate also increases the likelihood of a selection bias towards physicians who had either very positive or very negative perceptions of PrEP. Ambivalent physicians may have been overall less inclined to participate.

None of our studies also sought to explicitly explore migration and race as determinants of PrEP enthusiasm or as barriers to PrEP initiation. While questions pertaining to information available in different languages were asked, barriers related to race were not listed or inquired upon. While many new cases of HIV in Germany have been seen among new migrants, the cases of non-Germans who became infected with HIV outside of Germany are not included in the data regarding new HIV infections (59). Currently the most recent data concerning HIV infections are from 2020, which saw a direct reduction in caseloads likely due to a reduction in migration and a reduction in regular testing (59).

8. Conclusion

The studies performed all indicate a need for PrEP advisement from knowledgeable sources to increase access to PrEP. Our data from 2017 indicate a lack of communication between skilled advisors and those they seek to advise. Closing this gap with pamphlets, posts on social media or dating apps and engagement with influencers and bloggers can help ensure the correct information is available from the

sources patients already utilize. The coverage of PrEP by the statutory health insurances was a major step in reducing barriers to initiation for many patients across the PrEP spectrum, but ensuring they have someone in their area who can properly advise them is key. Additionally, working with demographics where moderate increases in new cases have been seen (i.e., heterosexual cisgender female sex workers and IV drug users) can help prevent future spikes and ensure they have a space in our HIV prevention program.

Physicians and counsellors themselves need simplified training programs and updated guidelines to improve their advisement skills. Ensuring SOPs are available in all local health departments can help prevent treatment gaps among patients who prefer not to go to counselling centers or who cannot afford counseling center prices for basic testing. Making sure patients are aware of their options and where they can make appointments for a PrEP initiation consultation are both essential to moving patients who could benefit from PrEP to a protective maintenance stage. Without ensuring this critical step, patients can fall into the black box within the PrEP continuum where they may decide not to start simply due to confusion as to what provider can offer them PrEP. Foreign patients who are less familiar with the German healthcare system, for example, would profit greatly from such clarity.

While physicians have a guideline that is published and now a way to bill the statutory health insurances for PrEP costs, there are still many hurdles and much confusion for many inexperienced providers. Physicians are due for a modern approach to training that helps increase engagement with PrEP licensure by decreasing barriers to receive PrEP billing accreditation. Utilizing methods we learned from the current pandemic can help decrease barriers to training, increase provider density across the country and ensure patients who want coverage are able to access it without undue stress.

Follow-up studies are needed to address more current needs of patients targeted in our papers. Additionally, including the breadth of patients across the PrEP spectrum (younger MSM, heterosexuals and IV drug users) will help identify current weak spots in providership and advisement. Looking to other countries' successes (i.e., opening GUM clinics that are open to all genders and sexual orientations or opting for less discriminatory risk assessment tools) can further support a widened, successful PrEP rollout.

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9. Affidavit/Statutory Declaration

“I, Mary K. Sammons, by personally signing this document in lieu of an oath, hereby affirm that I prepared the submitted dissertation on the topic ‘HIV Pre-exposure Prophylaxis Implementation in Germany: Barriers and Strategies to Improve Uptake’ (‘HIV-Präexpositionsprophylaxe in Deutschland: Barrieren und Strategien zur Verbesserung der Implementierung’) independently and without the support of third parties, and that I used no other sources and aids than those stated. All parts which are based on the publications or presentations of other authors, either in letter or in spirit, are specified as such in accordance with the citing guidelines.

The sections on methodology (in particular regarding practical work, laboratory regulations, statistical processing) and results (in particular regarding figures, charts and tables) are exclusively my responsibility.

My contributions to any publications to this dissertation correspond to those stated in the below joint declaration made together with the supervisor. All publications created within the scope of the dissertation comply with the guidelines of the ICMJE (International Committee of Medical Journal Editors; www.icmje.org) on authorship.

In addition, I declare that I am aware of the regulations of Charité – Universitätsmedizin Berlin on ensuring good scientific practice and that I commit to comply with these regulations.

The significance of this statutory declaration and the consequences of a false statutory declaration under criminal law (Sections 156, 161 of the German Criminal Code) are known to me.”

10. Declaration of contribution to the publications

Mary Sammons contributed the following to the below listed publications:

Publication 1: Werner RN, Gaskins M, Ahrens J, Jessen H, Kutscha F, Mosdzen R, Osswald W, Sander D, Schellberg S, Schwabe K, Wünsche T, Dressler C, **Sammons M**, Nast A. Knowledge and use of HIV pre-exposure prophylaxis among men who have sex with men in Berlin - A multicentre, cross-sectional survey. PloS one. 2018;13(9):e0204067-e. doi: 10.1371/journal.pone.0204067. PubMed PMID: 30212547.

I was responsible for data entry of the data collected via the paper questionnaires from offices across Berlin. I was involved in the discussion of results. I commented on the first draft of the publication and approved the final draft of the manuscript.

Journal Data Filtered By: **Selected JCR Year: 2018** Selected Editions: SCIE,SSCI Selected Categories: **"MULTIDISCIPLINARY SCIENCES"** Selected Category Scheme: WoS

Gesamtanzahl: 69 Journale

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	NATURE	745,692	43.070	1.285010
2	SCIENCE	680,994	41.037	1.070190
3	National Science Review	1,842	13.222	0.006500
4	Science Advances	21,901	12.804	0.110010
5	Nature Communications	243,793	11.878	1.103290
6	Nature Human Behaviour	1,230	10.575	0.006550
7	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	661,118	9.580	1.022190
8	Science Bulletin	3,569	6.277	0.009840
9	Scientific Data	3,240	5.929	0.015610
10	Frontiers in Bioengineering and Biotechnology	1,994	5.122	0.006540
11	Journal of Advanced Research	2,691	5.045	0.004780
12	Research Synthesis Methods	1,932	5.043	0.005420
13	GigaScience	2,674	4.688	0.012510
14	Annals of the New York Academy of Sciences	46,385	4.295	0.025840
15	Scientific Reports	302,086	4.011	1.061540
16	Journal of the Royal Society Interface	12,933	3.224	0.029190
17	NPJ Microgravity	203	3.111	0.000670
18	PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY A-MATHEMATICAL PHYSICAL AND ENGINEERING SCIENCES	19,227	3.093	0.028200

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
19	FRACTALS-COMPLEX GEOMETRY PATTERNS AND SCALING IN NATURE AND SOCIETY	1,429	2.971	0.001120
20	Journal of Radiation Research and Applied Sciences	860	2.963	0.001860
21	MIT Technology Review	929	2.893	0.001910
22	JOURNAL OF KING SAUD UNIVERSITY SCIENCE	1,120	2.835	0.001670
23	PROCEEDINGS OF THE ROYAL SOCIETY A-MATHEMATICAL PHYSICAL AND ENGINEERING SCIENCES	18,683	2.818	0.018940
24	PLoS One	650,727	2.776	1.706770
25	COMPLEXITY	2,753	2.591	0.003890
26	Royal Society Open Science	4,118	2.515	0.017150
27	PeerJ	11,911	2.353	0.045900
28	SCIENCE AND ENGINEERING ETHICS	1,719	2.275	0.003450
29	INTERNATIONAL JOURNAL OF BIFURCATION AND CHAOS	7,008	2.145	0.007390
30	Symmetry-Basel	2,097	2.143	0.002590
31	SCIENTIFIC AMERICAN	6,609	1.946	0.003540
32	Science of Nature	508	1.839	0.002000
33	PROCEEDINGS OF THE JAPAN ACADEMY SERIES B-PHYSICAL AND BIOLOGICAL SCIENCES	1,532	1.833	0.001960
34	Journal of Taibah University for Science	779	1.640	0.001240
35	Frontiers in Life Science	241	1.622	0.000500
36	ARABIAN JOURNAL FOR SCIENCE AND ENGINEERING	3,838	1.518	0.005840
37	SCIENCE PROGRESS	521	1.500	0.000400

PLOS ONE

RESEARCH ARTICLE

Knowledge and use of HIV pre-exposure prophylaxis among men who have sex with men in Berlin – A multicentre, cross-sectional survey

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Citation: Werner RN, Gaskins M, Ahrens J, Jessen H, Kutscha F, Mosdzen R, et al. (2018) Knowledge and use of HIV pre-exposure prophylaxis among men who have sex with men in Berlin – A multicentre, cross-sectional survey. PLoS ONE 13 (9): e0204067. https://doi.org/10.1371/journal.pone.0204067

Editor: Jesse L. Clark, David Geffen School of Medicine at UCLA, UNITED STATES

Received: July 23, 2018

Accepted: August 31, 2018

Published: September 13, 2018

Data Availability Statement: The minimal underlying data set and codebook have been uploaded as a supplementary file. The age of the respondents and qualitative data have been removed to ensure patient anonymity.

Funding: The authors received no specific funding for this work.

Competing interests: I have read the journal's policy and the authors of this manuscript have the following competing interests: The authors RNW,

Abstract

Background

HIV pre-exposure prophylaxis (PrEP) has likely contributed to large decreases in HIV incidence among men who have sex with men (MSM) in several major cities. Berlin has seen a smaller decline, and affordable PrEP has been accessible through formal channels in Germany only since autumn 2017. We aimed to investigate knowledge and use of PrEP among MSM in Berlin, and factors predictive of a desire to use PrEP and history of PrEP use.

Methods

Multicentre, paper-based, self-administered survey of adult MSM whose HIV status was negative or unknown at time of participation. Data were collected from 1 October 2017 to 2 April 2018.

Results

473 of 875 questionnaires were returned (response rate 54.1%; mean age 37.4 years, range 18–79). 90.0% of participants were aware of PrEP and, of these, 48.2% felt well informed about it. Among the 17.2% of participants reporting PrEP use, 59.3% indicated obtaining some or all of it from informal sources. 23.7% of those with no history of PrEP use reported having condomless anal intercourse (CAI) with two or more partners over the past six months. Worries about side effects, cost, not having a doctor who prescribes it, and a lack of information were the most frequently reported barriers to PrEP use. A desire to use PrEP and history of PrEP use were associated in our multivariable model with having

MG, JA, FK, RM, WO, DS, TW, CD, MS, and AN have declared that no competing interests exist. HJ received payments for research from Gilead Sciences GmbH; for Board membership from Gilead Sciences GmbH, MSD and ViiV Healthcare GmbH; for speaker activities from ViiV Healthcare GmbH, Abbvie Deutschland GmbH & Co. KG, Gilead Sciences GmbH, Gilead Sciences Ltd; and for travel/accommodation/meeting expenses from ViiV Healthcare GmbH, Abbvie Deutschland GmbH & Co. KG, Gilead Sciences GmbH, Gilead Sciences Ltd. SS declares that he received honoraria and support for lectures on the topic discussed in this paper by various commercial and non-commercial entities. The authors FK and KS are affiliated with Schwulenberatung Berlin gGmbH. The Schwulenberatung Berlin is not a commercial entity. Its gGmbH status allows it to accept private donations in addition to state funding. The funding of the Schwulenberatung Berlin comes primarily from the Berlin state government. Please see the following web link in English: http://www.schwulenberatungberlin.de/post.php?permalink=financing#seitenanfang. There are no patents, products in development or marketed products to declare. This does not alter our adherence to all the PLOS ONE policies on sharing data and materials.

multiple CAI partners. A history of PrEP use was associated with having a university degree, one or two parents born outside Germany, or friends living with HIV.

Conclusions

We found high awareness of PrEP among MSM in Berlin, but also a strong need for more education on its pros, cons and proper use. The frequency of informal PrEP use was also high, raising urgent individual and public health concerns. Policy makers need to consider recent calls to improve access to PrEP and PrEP education through regular health services.

Introduction

HIV pre-exposure prophylaxis, or PrEP, is a biomedical form of HIV prevention that has demonstrated high efficacy and safety in clinical trials [1–4] and cohort studies [5–15]. In 2017 the Centers for Disease Control and Prevention (CDC) in the United States issued an updated clinical practice guideline recommending PrEP for men who have sex with men (MSM) and who report having had a bacterial sexually transmitted infection (STI), anal sex without condoms outside a monogamous relationship with an HIV-negative partner, or both within the past six months [16]. The results of a modelling study from 2016 suggest that achieving 40% coverage of indicated MSM would avert 33% of infections expected in the US over the next decade [17]. Indeed, increased use of PrEP is thought to have already contributed to substantial declines in HIV incidence among MSM in London [18], San Francisco [19] and New South Wales, Australia [20].

To become an effective part of HIV prevention strategies, PrEP must be made accessible to the populations at highest risk of HIV infection, such as MSM. However, while awareness of PrEP among MSM is generally increasing [21–25], it varies widely across geographies [26,27], as well as socioeconomic and ethnic groups [28,29]. Likewise, the willingness of MSM to use PrEP is influenced by various factors, including cost, perceived level of protection against HIV infection, adverse effects and socioeconomic status [30–32].

In Germany, the incidence of HIV among MSM has decreased since 2013, falling from 2500 new cases that year to an estimated 2100 in 2016 [33]. This decline has been attributed primarily to the use of HIV treatment as a form of prevention [33]. Around 20% of new cases of HIV among MSM in Germany in 2016 were diagnosed in immigrants, with central Europe, western Europe and South America being the most frequent regions of origin [34]. The German states with the highest HIV incidence were the city-states of Berlin and Hamburg, both of which saw 10.1 new cases of HIV per 100,000 population compared to an incidence of 4.2 per 100,000 in Germany as a whole [34].

Berlin joined the Fast-Track Cities initiative of the Joint United Nations Programme on HIV/AIDS (UNAIDS) in 2016 and, in doing so, committed to attain the 90-90-90 and zero stigma and discrimination targets. In addition to its major goal of rapidly expanding the use of HIV treatment as a highly effective form of prevention [35], the initiative recommends improved and more widespread implementation of other preventive strategies, such as PrEP [36]. The current Berlin state government is planning a model project to deliver free PrEP services to a limited number of people who are not able to afford these themselves [37], satisfying some of the demands of local HIV counselling centres and NGOs [38].

Despite these commitments and plans, very little information is available on what MSM in Germany know about PrEP, the extent to which and how they use it, and the attitudes they

have towards it. In particular, there is no information of this nature specifically for Berlin. The aim of our study was therefore to survey MSM attending HIV specialist practices or HIV testing and counselling centres on these topics and to identify barriers, enablers and other factors associated with participants' desire to use PrEP and any history of PrEP use. Data of this nature from Berlin can provide a useful comparison to the situation in cities such as London or Paris, where the implementation of PrEP is already well underway.

Materials and methods

Study design

We conducted a cross-sectional, multicentre survey of MSM attending HIV specialist practices or HIV testing and counselling centres in Berlin using an anonymous, self-administered, paper-based questionnaire. The study protocol was approved by the institutional ethics committee of Charité–Universitätsmedizin Berlin (EA1/162/17, 28 September 2017). Participation was voluntary and all participants gave verbal informed consent in English or German before filling in the questionnaire. We did not provide any incentives to the centres or participants to take part in the study.

Sampling methods and settings

MSM were eligible to take part in the survey if they were aged 18 years or older and had a self-reported negative or unknown HIV serostatus at the time of participation. Data were collected from 1 October 2017 to 2 April 2018. Because we aimed to recruit a heterogeneous sample of MSM in Berlin, we collected data in various settings: HIV and STI testing and counselling centres for MSM and HIV specialist practices. The former are walk-in centres offering low-threshold, anonymous counselling on legal and health issues, as well as testing for HIV and STIs. They are not permitted to prescribe medication. We invited all of these centres in Berlin (n = 4) to participate in our study. HIV specialist practices in Berlin are owned and staffed by doctors, and visiting them usually requires an appointment. They provide a range of generalist and sexual health care to LGBTI+ people whether or not they are living with HIV. We invited a total of 11 such practices from seven different neighbourhoods across Berlin to participate in our study. These were chosen purposively based on their geographic spread and our knowledge that they had participated in other research related to HIV.

Counsellors invited eligible clients to participate in the survey if they were seeking STI or HIV tests or counselling. Patients at the HIV specialist practices were selected by participating doctors, who had been asked to include every eligible patient consecutively regardless of the reason for the patient consultation. The questionnaire was prefaced with information about PrEP and our survey.

Content and format of the questionnaire

We designed a two-page questionnaire consisting mostly of closed multiple-choice questions with single or multiple answers allowed. The questions covered the following topics, all of which focused on the perspective of the participating MSM:

- awareness of PrEP and sources of information about it;
- desire to use PrEP and history of PrEP use;
- barriers to PrEP use, including perceived risks;
- preferences for dosage regimen and route of administration;

- anticipated impact of taking PrEP on the participants' use of condoms; and
- attitudes towards pricing and reimbursement through public insurance.

In addition, we asked questions about participants' sexual behaviour and HIV risk (date of last HIV test, diagnosis of any STI in the past six months, role in anal sex, number of anal sex partners in the past six months, number of anal sex partners without condoms in the past six months). We also collected sociodemographic data (age, place of residence, education, financial situation and family origins). The last of these variables was chosen to capture information on whether participants had a family or personal history of immigration to Germany.

Additionally, the questionnaire contained an open-ended question focusing on the motivation behind participants' use of, or desire to use, PrEP. These data will be reported elsewhere. The questionnaire was available in German and English, and the full versions are available as supporting information (S1 and S2 Files).

Sample size and statistical methods

No formal sample size calculations were performed. Based on considerations of feasibility, we aimed to collect data from 400 to 600 participants. We used descriptive statistics to summarise sample characteristics and Pearson's chi-squared test to measure the association among pre-selected categorical variables. For the latter analyses, we applied a Bonferroni-adjustment to account for multiple testing (alpha level at 0.005). Additionally, we used multivariable logistic regression to identify predictors of having a desire to use PrEP or a history of PrEP use. Odds ratios and their respective 95% confidence intervals were used to quantify the effects. To select variables for our multivariable model, we compiled the following initial working set of potential predictors in which we had a priori interest based on background knowledge: age, financial situation, education, family origins, sexual risk behavior, self-perceived risk, having peers living with HIV, and perceived barriers and risks of PrEP. For pragmatic reasons of reporting and traceability, we subsequently screened these using simple (i.e., univariable) logistic regression and included in the multivariable model those variables that were associated with the respective dependent variable at a p-value cut-off point of 0.075 following the approach described by Bursac et al. [39]. We later conducted a sensitivity analysis with all variables of a priori interest to ensure that important adjustment variables had not been overlooked. Missing cases were excluded in a listwise fashion.

To avoid collinearity of independent variables related to different measures of sexual risk behaviour in our logistic regression models, we created a new variable comprising four groups as shown in Table 1. In doing so, we aimed to approximate roughly the indications for PrEP use recommended by the CDC for MSM. We chose "two or more partners" rather than "one" as our cut-off point to account for the possibility that participants who reported condomless

Table 1. Definitions of sexual risk behaviour groups, according to self-reported number of condomless anal intercourse partners and diagnosis of any sexually transmitted infection over the past six months.

Label for sexual risk behaviour	Definitions (referring to the past six months)
"Highest risk (CAI + STI)"	Reported having had CAI with two or more partners and a diagnosis of any STI
"Higher risk (CAI)"	Reported having had CAI with two or more partners but no STI diagnosis
"Higher risk (STI)"	Reported having had a diagnosis of any STI but not CAI with two or more partners
"Low risk"	Did not report having had an STI diagnosis or CAI with two or more partners

CAI, condomless anal intercourse; STI, sexually transmitted infection.

https://doi.org/10.1371/journal.pone.0204067.t001

anal intercourse (CAI) with one partner might be describing CAI within a monogamous partnership. We did not distinguish between receptive or insertive CAI because the CDC indications for PrEP use for MSM do not do so either.

IBM SPSS Version 22 was used for the descriptive statistics and cross-tabulations, whereas Stata SE 14.2 (StataCorp) was used to estimate the regression models.

Results

All of the HIV and STI testing and counselling centres in Berlin (n = 4) chose to participate in the study. Of the 11 HIV specialist practices invited to participate, a total of six elected to take part. The participating centres handed out 875 questionnaires, of which 473 were returned, yielding a response rate of 54.1%. We excluded three participants because they had indicated in the questionnaire that they were living with HIV. This left 470 questionnaires for further analysis.

Demographic data

Of the 470 questionnaires in our analysis sample, 84.9% were in German. The mean age of the participants was 37.4 years (SD: 11.9; range: 18–79 years), and 94.0% indicated that they lived in Berlin. Around two-thirds (65.3%) of the participants had a university degree, and 87.4% described their financial situation as having "enough money" or "more than enough money" to pay for the things they need. One third of the participants reported either that one or two of their parents (14.9%) or that they themselves (23.8%) had been born outside Germany. One quarter of the participants (24.9%) stated that they had no friends or acquaintances living with HIV, whereas 35.5% and 49.6% reported having acquaintances or friends living with HIV, respectively.

Sexual risk behaviour

Referring to the past six months, 17.4% of the participants stated that they had been diagnosed with an STI, 68.1% that they had had anal sex with two or more partners, and 32.1% that they had had anal sex with two or more partners without using a condom, respectively. According to our sexual risk behaviour stratification, 58.9% were categorized as "low risk", 6.4% as "higher risk (STI)"‘, 22.1% as "higher risk (CAI)", and 11.1% as "highest risk (CAI + STI)". Seven participants could not be assigned to a category due to missing information for either the number of CAI partners or the diagnosis of an STI in the past six months. Among participants who reported never having used PrEP, almost one quarter (90/379) indicated that they had had CAI with two or more partners in the past six months.

When asked whether the sex they have is always as safe as they would like it to be, 66.0% of all participants agreed or strongly agreed with the statement and 18.9% disagreed or strongly disagreed. Table 2 gives an overview of the demographic and sexual risk behaviour data.

Awareness of PrEP and sources of information

In total, 90% of participants (n = 423) reported already being aware of PrEP. Of these, 48.2% agreed or strongly agreed with the statement that they were well informed about PrEP, whereas 31.9% disagreed or strongly disagreed. Their sources of knowledge about PrEP (multiple answers allowed) were friends or acquaintances (61.7%), magazines, journals or blogs (57.4%), dating apps or platforms (34.0%), doctors (22.7%), counselling centres (13.9%), and others (10.6%). Doctors were named as a source of information about PrEP significantly more often by participants in the "highest risk (CAI + STI)" sexual risk behaviour category than by other

Table 2. Demographic data and sexual risk behaviour; total sample and subsamples according to type of centre.

		Total sample	Type of centre	
			Counselling centres[1]	Doctor practices[2]
N		470	221	249
Age				
	Mean (SD)	37.4 (11.9)	32.9 (8.0)	41.4 (13.2)
	Min; Max	18–79	18–59	19–79
Highest degree or level of school (N, %)				
	Primary education	0	0	0
	Secondary education up to year 10*	42 (8.9%)	8 (3.6%)	34 (13.7%)
	Secondary education with apprenticeship	23 (4.9%)	5 (2.3%)	18 (7.2%)
	Secondary education up to year 12**	89 (18.9%)	44 (19.9%)	45 (18.1%)
	University degree	307 (65.3%)	160 (72.4%)	147 (59.0%)
	Not stated	9 (1.9%)	4 (1.8%)	5 (2.0%)
Financial situation (N, %)				
	Not always enough money	51 (10.9%)	23 (10.4%)	28 (11.2%)
	Enough money	205 (43.6%)	95 (43.0%)	110 (44.2%)
	More than enough money	206 (43.8%)	99 (44.8%)	107 (43.0%)
	Not stated	8 (1.7%)	4 (1.9%)	4 (1.6%)
Place of residence (N, %)				
	Berlin	442 (94.0%)	204 (92.3%)	238 (95.6%)
	Other city in Germany	10 (2.1%)	4 (1.8%)	6 (2.4%)
	Small town / rural area in Germany	4 (0.9%)	3 (1.4%)	1 (0.4%)
	Other country	8 (1.7%)	7 (3.2%)	1 (0.4%)
	Not stated	6 (1.3%)	3 (1.4%)	3 (1.2%)
Family origins (N, %)				
	Participants & both parents born in Germany	281 (59.8%)	112 (50.7%)	169 (67.9%)
	One parent born outside Germany	32 (6.8%)	19 (8.6%)	13 (5.2%)
	Both parents born outside Germany	38 (8.1%)	25 (11.3%)	13 (5.2%)
	Participant born outside Germany	112 (23.8%)	62 (28.1%)	50 (20.1%)
	Not stated	7 (1.5%)	3 (1.4%)	4 (1.6%)
Current HIV status (N, %)				
	HIV negative	406 (86.4%)	171 (77.4%)	235 (94.4%)
	Not sure	52 (11.1%)	41 (18.6%)	11 (4.4%)
	Not stated	12 (2.6%)	9 (4.1%)	3 (1.2%)
STI diagnosis in the past six months (N, %)				
	No	381 (81.1%)	183 (82.8%)	198 (79.5%)
	Yes	82 (17.4%)	34 (15.4%)	48 (19.3%)
	Not stated	7 (1.5%)	4 (1.8%)	3 (1.2%)
Role when having anal sex (N, %)				
	No anal sex	21 (4.5%)	2 (0.9%)	19 (7.6%)
	Bottom only	37 (7.9%)	19 (8.6%)	18 (7.2%)
	More bottom than top	91 (19.4%)	48 (21.7%)	43 (17.3%)
	Top and bottom (versatile)	141 (30.0%)	66 (29.9%)	75 (30.1%)
	More top than bottom	99 (21.1%)	47 (21.3%)	52 (20.9%)
	Top only	72 (15.3%)	33 (14.9%)	39 (15.7%)
	Not stated	9 (1.9%)	6 (2.7%)	3 (1.2%)
Number of anal sex partners in the past six months (N, %)				

(*Continued*)

Table 2. (Continued)

		Total sample	Type of centre	
			Counselling centres[1]	Doctor practices[2]
	None	55 (11.7%)	10 (4.5%)	45 (18.1%)
	1	80 (17.0%)	36 (16.3%)	44 (17.7%)
	2 to 5	142 (30.2%)	85 (38.5%)	57 (22.9%)
	6 to 10	79 (16.8%)	38 (17.2%)	41 (16.5%)
	More than 10	99 (21.1%)	45 (20.4%)	54 (21.7%)
	Not stated	15 (3.2%)	7 (3.2%)	8 (3.2%)
Number of anal sex partners without using condom in the past six months (N, %)				
	None	174 (37.0%)	68 (30.8%)	106 (42.6%)
	1	134 (28.5%)	79 (35.7%)	55 (22.1%)
	2 to 5	109 (23.2%)	50 (22.6%)	59 (23.7%)
	6 to 10	23 (4.9%)	10 (4.5%)	13 (5.2%)
	More than 10	19 (4.0%)	6 (2.7%)	13 (5.2%)
	Not stated	11 (2.3%)	8 (3.6%)	3 (1.2%)

STI, sexually transmitted infection.

[1]Counselling centres: Fixpunkt e.V., Mann-O-Meter e.V., Berliner AIDS-Hilfe e.V., Pluspunkt / Schwulenberatung Berlin gGmbH (listed in descending order according to number of returned questionnaires).

[2]Practices: Gemeinschaftspraxis Dietmar Schranz und Klaus Fischer, Praxis Jessen[2] + Kollegen, Praxis Wünsche, Ärztezentrum Nollendorfplatz, Praxiszentrum Kaiserdamm, Novopraxis Berlin GbR (listed in descending order according to number of returned questionnaires).

*or similar.

**for example A levels, high school diploma, German "Abitur".

https://doi.org/10.1371/journal.pone.0204067.t002

participants (42.3% vs. 18.4%, p<0.001). This was not the case with counselling centres, however (17.3% vs. 12.1%, p = 0.291).

Barriers to PrEP use

Two-thirds (65.6%) of the survey participants agreed or strongly agreed with the statement that PrEP is a safe way to prevent infection with HIV. Agreement was significantly more common among participants who had indicated that they were well informed about PrEP (p<0.001). Participants attributed the following risks to the use of PrEP (multiple answers allowed): A higher risk of getting infected with other STIs (64.3%), mild or temporary side effects (43.6%), severe or permanent side effects (19.8%), a higher risk of getting infected with HIV (6.2%), and other risks (5.1%). After we applied a Bonferroni-adjusted alpha-level (p<0.005) to account for multiple comparisons across survey items, however, the only differences between the well-informed versus not- well-informed groups that remained significant were those for the items "Higher risk of getting infected with other STIs" and "Not sure" (Table 3).

Among participants without a history of PrEP intake (n = 387), the following were named as circumstances under which they would consider using PrEP (multiple answers allowed): if they had fewer worries about side effects (47.3%), if it were cheaper (39.8%), if a doctor prescribed it (31.8%), if they had more information (31.3%), and other circumstances (3.7%).

Desire to use PrEP

Among participants with no history of PrEP use (n = 387), 42.4% agreed or strongly agreed with the statement that they would like to use PrEP themselves, whereas 34.8% disagreed or

Table 3. Participants' perception of risks of PrEP use, by self-reported level of knowledge about PrEP.

What risks do you see for people who use PrEP? (multiple answers allowed)			
	"I am well informed about PrEP"		p value[$]
	Agree or strongly agree (N = 210)	Disagree or strongly disagree (N = 166)	
None	10 (4.8%)	2 (1.2%)	0.051
Mild / temporary side effects	106 (50.5%)	64 (38.6%)	0.021
Severe / permanent side effects	40 (19.0%)	36 (21.7%)	0.527
Higher risk of getting infected with HIV	8 (3.8%)	14 (8.4%)	0.058
Higher risk of getting infected with other STIs	156 (74.3%)	96 (57.8%)	0.001
Other risks	14 (6.7%)	4 (2.4%)	0.055
Not sure	7 (3.3%)	41 (24.7%)	< .001

STI, sexually transmitted infection.

[$]From Chi-squared tests of the null hypothesis that there is a no significant difference between the expected frequencies and the observed frequencies in the categories.

https://doi.org/10.1371/journal.pone.0204067.t003

strongly disagreed. In our univariable logistic regression models, the following variables were significantly positively associated with the desire to take PrEP: belonging to the "higher risk (CAI)" or "highest risk (CAI + STI)" categories for sexual risk behaviour; perceived riskiness of own sexual behaviour; and expressing the need to have a doctor who prescribed PrEP. Attributing to PrEP a higher risk of getting infected with STIs was significantly negatively associated with the desire to take PrEP. In our multivariable model, the following factors were significant positive predictors of the desire to take PrEP: belonging to the "higher risk (CAI)" or the "highest risk (CAI + STI)" category; and having expressed the need to have a doctor who prescribed PrEP. The one significant negative predictor was having attributed to PrEP a higher risk of getting infected with other STIs (Table 4). A response tree for the multivariable regression model for the desire to use PrEP is shown in Fig 1.

History of PrEP use and sources of PrEP

The majority of participants (82.3%) had never used PrEP themselves. Of the 81 (17.2%) who had, 46.9% reported using it continuously, 13.6% using it on-demand and 39.5% using or having used it but not on a regular basis. Asked about the source of their PrEP (multiple answers allowed), 44.4% of the 81 participants reported obtaining a prescription from their doctor, 35.8% importing it from another country, 18.5% using pills originally prescribed for post-exposure prophylaxis (PEP), 11.1% using pills from a friend's HIV medication, and 4.9% using other ways to obtain the medication. Only 32.1% of participants who had a history of PrEP intake reported using a private prescription as their only source of PrEP, and 59.3% reported that they had obtained some or all of their PrEP by means other than a private prescription. This latter number rises to 64.8% if we exclude those who did not answer this question (n = 7).

In our univariable logistic regression models, the following variables were significantly positively associated with a history of PrEP use: having a university degree, having been born outside of Germany, belonging to the "higher risk (CAI)" or the "highest risk (CAI + STI)" category, having friends or acquaintances living with HIV, and attributing to PrEP a higher risk of infection with other STIs. In our multivariable analysis, belonging to the "higher risk (CAI)" or "highest risk (CAI + STI)" sexual risk behaviour category was a strong positive predictor of having a history of PrEP use. Further positive predictors were having a university

Table 4. ORs and 95% CIs for expressing a desire to use PrEP, by sexual risk behaviour, perceived riskiness of own sexual behaviour, and barriers and risks attributed to PrEP intake.

			Participants expressing a desire to use PrEP		Crude OR	Adjusted OR[†]
Participant characteristics		**N[‡]**	***n* (%)**	***p* value[§]**	**(95% CI)**	**(95% CI)**
Sexual risk behaviour (past six months)				<0.001		
	No STI; no multiple* CAI partners	193	86 (44.6%)		Reference	Reference
	STI; no multiple* CAI partners	17	7 (41.2%)		0.85 (0.31–2.33)	1.02 (0.34–3.05)
	No STI; multiple* CAI partners	66	52 (78.8%)		4.58 (2.33–9.00)	3.77 (1.84–7.69)
	STI; multiple* CAI partners	20	19 (95.0%)		23.07 (3.03–175.93)	17.22 (2.18–136.14)
Perceived riskiness of own sexual behaviour: "When I have sex, it is always as safe as I'd like it to be"				<0.001		
	Strongly disagree	9	6 (66.7%)		Reference	Reference
	Disagree	51	39 (76.5%)		1.27 (0.22–7.39)	2.16 (0.4–11.64)
	Neither agree nor disagree	37	27 (73.0%)		1.16 (0.19–7.04)	2.63 (0.46–14.94)
	Agree	123	64 (52.0%)		0.44 (0.08–2.37)	1.31 (0.26–6.44)
	Strongly agree	73	27 (37.0%)		0.23 (0.04–1.28)	0.77 (0.15–3.90)
"If a doctor prescribed it"				0.012		
	Not selected as a circumstance under which participant would use PrEP	202	99 (49.0%)		Reference	Reference
	Selected as a circumstance under which participant would use PrEP	97	65 (67.0%)		1.96 (1.17–3.28)	2.44 (1.36–4.37)
"A higher risk of getting infected with HIV"				0.078		
	Not selected as risk seen for people using PrEP	282	158 (56.0%)		Reference	Reference
	Selected as risk seen for people using PrEP	16	5 (31.3%)		0.38 (0.13–1.14)	0.34 (0.10–1.11)
"A higher risk of getting infected with other STIs"				0.053		
	Not selected as risk seen for people using PrEP	120	76 (63.3%)		Reference	Reference
	Selected as risk seen for people using PrEP	178	87 (48.9%)		0.53 (0.32–0.87)	0.54 (0.31–0.92)

CAI, condomless anal intercourse; CI, confidence interval; OR, odds ratio; PrEP, HIV pre-exposure prophylaxis; STI, sexually transmitted infection. P-values from joint Wald tests of the null hypothesis that there is no variation across a category for the univariate and multivariate regression models were <0.0001 and 0.0002 for sexual risk behaviour, <0.0001 and 0.0576 for perceived riskiness of own sexual behaviour, 0.0095 and 0.0028 for doctor prescription as a pre-condition for PrEP use, 0.074 and 0.0748 for attributing to PrEP a higher risk of getting infected with HIV, and 0.0105 and 0.0243 for attributing to PrEP a higher risk of getting infected with other STIs, respectively.

[†]Multivariable analysis adjusting for sexual risk behaviour, perceived riskiness of own sexual behaviour, having a doctor who prescribes PrEP, and risk of HIV and STI attributed to PrEP intake.

[‡]The sample excludes patients who were missing information on the relevant variables. Fig 1 gives an overview of participants included and excluded in the regression model.

[§]From Chi-squared tests of the null hypothesis that there is a no significant difference between the expected frequencies and the observed frequencies in one or more categories (e.g., across sexual risk behaviour groups).

*"multiple" was defined as reporting having had two or more CAI partners in the past six months.

https://doi.org/10.1371/journal.pone.0204067.t004

degree, one or two parents born outside of Germany, and friends or acquaintances living with HIV, as well as attributing to PrEP a higher risk of infection with other STIs (Table 5). A response tree for the multivariable regression model for history of PrEP use is shown in Fig 2.

Anticipated impact of PrEP on participants' use of condoms

When asked about the extent to which they agreed with the statement that they had (or would have) anal sex without a condom more often when taking PrEP, 45.4% of the participants agreed or strongly agreed whereas 33.0% disagreed or strongly disagreed. Participants who expressed a desire to use PrEP and those who stated that they were using or had used PrEP were significantly more likely to agree with the statement than other participants (Table 6).

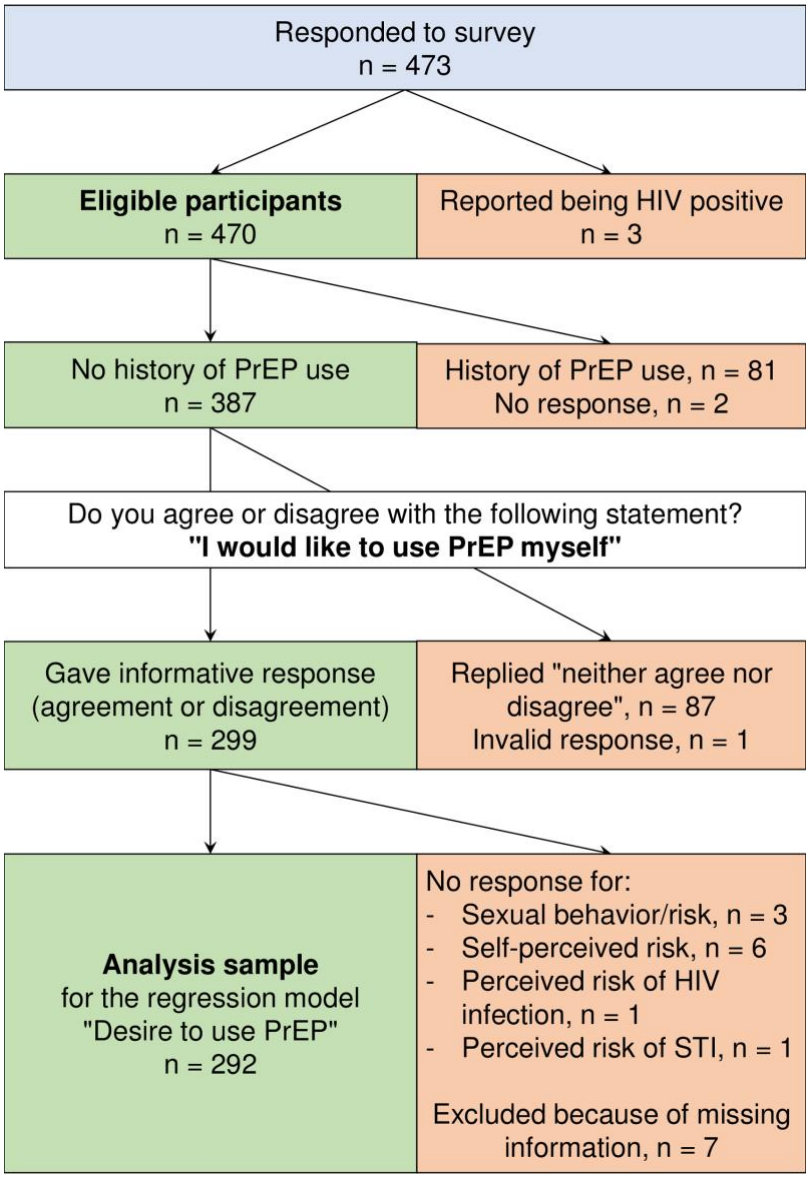

Fig 1. Response tree for the multivariable regression model of desire to use PrEP.

https://doi.org/10.1371/journal.pone.0204067.g001

Table 5. ORs and 95% CIs for having a history of PrEP use, by education, family origins, sexual risk behaviour, having friends or acquaintances living with HIV, and risks attributed to PrEP use.

		Participants who had a history of PrEP use		Crude OR	Adjusted OR[†]
Participant characteristics	***N*[‡]**	***n* (%)**	***p* value[§]**	**(95% CI)**	**(95% CI)**
Education			0.014		
No university degree	154	16 (10.4%)		Reference	Reference
University degree	305	61 (20.0%)		2.21 (1.21–-4.04)	2.44 (1.22–4.91)
Family origins			0.031		
Participant and parents born in Germany	279	37 (13.3%)		Reference	Reference
One or two parents born outside Germany	70	17 (24.3%)		1.92 (0.98–3.78)	3.03 (1.37–6.73)
Participant born outside Germany	112	24 (21.4%)		1.82 (1.02–3.24)	1.80 (0.90–3.60)
Sexual risk behaviour (past six months)			<0.001		
No STI; no multiple* CAI partners	276	18 (6.5%)		Reference	Reference
STI; no multiple* CAI partners	30	0 (0.0%)		Empty	Empty
No STI; multiple* CAI partners	103	31 (30.1%)		6.92 (3.57–13.43)	7.25 (3.64–14.45)
STI; multiple* CAI partners	52	29 (55.8%)		19.10 (9.04–40.35)	16.18 (7.37–35.53)
Having friends or acquaintances living with HIV			<0.001		
No	116	5 (4.3%)		Reference	Reference
Yes	344	73 (21.2%)		5.66 (2.22–14.41)	4.16 (1.53–11.37)
"A higher risk of getting infected with STIs"			0.013		
Not selected as risk seen for people using PrEP	165	17 (10.3%)		Reference	Reference
Selected as risk seen for people using PrEP	302	64 (21.2%)		2.35 (1.28–4.30)	2.77 (1.39–5.52)

CAI, condomless anal intercourse; CI, confidence interval; OR, Odds ratio; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection. P-values from joint Wald tests of the null hypothesis that there is no variation across a category for the univariate regressions and the multivariate regression model were 0.0068 and 0.0120 for education, 0.0537 and 0.0170 for family origins, < .0001 and < .0001 for sexual risk behaviour, <0.0001 and 0.0054 for having friends or acquaintances living with HIV, and 0.0034 and 0.0039 for attributing PrEP a higher risk of getting infected with STIs, respectively.

[†]Multivariable analysis adjusting for education, family origins, sexual risk behaviour, having friends or acquaintances living with HIV, and risk of STI attributed to PrEP intake.

[‡]The sample excludes patients who were missing information on the relevant variables. Fig 2 gives an overview of participants included and excluded in the regression model.

[§]From Chi-squared tests of the null hypothesis that there is a no significant difference between the expected frequencies and the observed frequencies in one or more categories (e.g., across sexual risk behaviour groups).

*"multiple" was defined as reporting having had two or more CAI partners in the past six months.

https://doi.org/10.1371/journal.pone.0204067.t005

Attitudes towards insurance coverage and pricing of PrEP

The majority of participants stated that the cost of PrEP should be covered by public health insurance in Germany, either for all MSM who want to use PrEP (64.7%) or only for MSM at the highest risk of acquiring HIV (13.4%). For the majority of participants (59.1%), an acceptable price per month if PrEP were never to be covered by public health insurance was 50 euros or less, followed by 100 euros or less for 21.3%, and 200 euros or less for 6.2%.

Discussion

Our study is the first to use a facility-based survey to investigate what MSM in Berlin know about PrEP, the extent to which and how they use it, and the attitudes they have towards it.

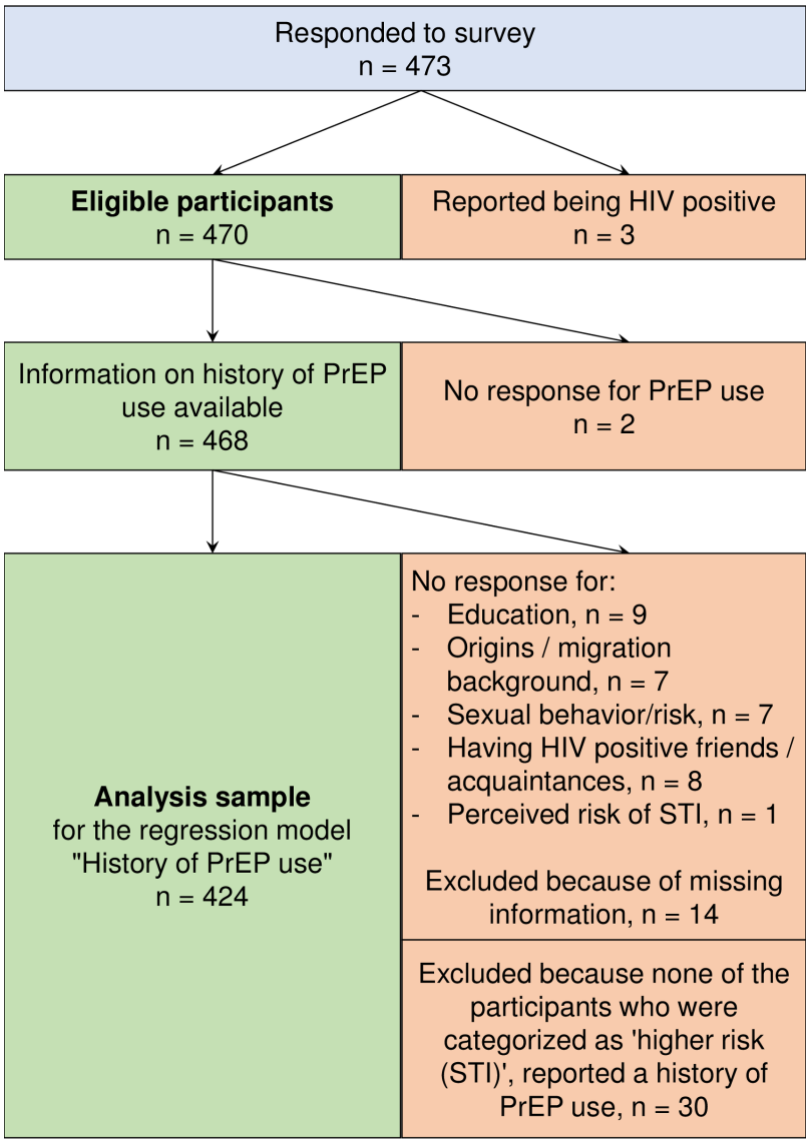

Fig 2. Response tree for the multivariable regression model for history of PrEP use.

https://doi.org/10.1371/journal.pone.0204067.g002

Table 6. Anticipated impact of taking PrEP on participants' use of condoms, by desire to use PrEP and history of PrEP use.

"I have (or would have) anal sex without a condom more often when taking PrEP"						
	"I would like to use PrEP myself"		p value[$]	*History of PrEP use*		p value[$]
	Agree or strongly agree (N = 207)	Neutral, disagree or strongly disagree (N = 211)		Yes (N = 80)	No (N = 372)	
Strongly disagree	18 (8.7%)	58 (27.5%)	< .001	7 (8.8%)	77 (20.7%)	0.002
Disagree	36 (17.4%)	32 (15.2%)		7 (8.8%)	64 (17.2%)	
Neither agree nor disagree	23 (11.1%)	38 (18.0%)		8 (10.0%)	55 (14.8%)	
Agree	79 (38.2%)	64 (30.3%)		37 (46.3%)	116 (31.2%)	
Strongly agree	39 (18.8%)	13 (6.2%)		17 (21.3%)	42 (11.3%)	
I never use condoms anyway	12 (5.8%)	6 (2.8%)		4 (5.0%)	18 (4.8%)	

[$]From Chi-squared tests of the null hypothesis that there is a no significant difference between the expected frequencies and the observed frequencies in the categories.

https://doi.org/10.1371/journal.pone.0204067.t006

We additionally sought to identify factors associated with participants' willingness to use PrEP and any history of PrEP use.

With data provided by almost 500 MSM in Berlin with a self-reported negative or unknown HIV serostatus, we found that awareness of PrEP, at 90%, was very high. However, fewer than half of those who were aware of PrEP felt well informed about it. This is troubling given that at least 60% of participants who were currently on PrEP or had used it at some point in the past reported that they had obtained some or all of their medication from an informal source, such as imports, pills originally prescribed for PEP or a friend's HIV medication. The individual and public health risks of informal PrEP use are manifold and include delays in identifying side effects and infections with other STIs, an increased risk of HIV infection, and the development of drug resistant HIV strains that can be transmitted to others and harder to treat. To address this situation it will be crucial for policy makers in Germany to consider recent calls from the German STI Association (DSTIG) and the DAIG to improve access to PrEP and PrEP education through regular health care services [40,41]. As of July 2018, public health insurance in Germany did not cover the cost of PrEP medication or any related diagnostic tests or patient education specifically related to PrEP.

The importance of being able to obtain PrEP through formal channels is further supported by another of our findings, namely that participants who reported that they were taking PrEP in a manner consistent with the evidence (i.e., regularly or on-demand) were significantly more likely to have obtained a prescription from their doctor. Indeed, reliable information on PrEP would appear to be an important enabler of its proper use considering that participants who felt they were well informed about PrEP were better at identifying the true risks associated with it. More generally, the likelihood of having a history of PrEP use was associated in our regression model with having a university degree and with having friends or acquaintances who are living with HIV. Information may play a role as an enabler in both scenarios if we assume that MSM who have a university degree may have better access to health information or seek it out more assertively than those who do not. Likewise, it is possible that being part of a social network in which people communicate more openly about HIV leads to greater awareness of the disease and facilitates access to information about HIV medication and prevention.

Conversely, a lack of information was cited as a barrier to PrEP use by almost one third of participants who had no history of PrEP intake. Given that almost half of this group also indicated that they would consider using PrEP if they had fewer worries about side effects, it would seem that efforts to improve PrEP education in Germany should focus on the potential side effects of PrEP therapy in addition to emphasising the importance of adherence and regular diagnostic testing.

The most frequent sources of information about PrEP for our participants were their friends and acquaintances, as well as magazines, blogs and dating apps. This is unsurprising given evidence pointing to the important role of word-of-mouth communication when people make health-related decisions [42]. Given the high proportion of informal PrEP use suggested by our data, however, the fact that only a quarter of MSM in our sample reported doctors as one of their sources of information about PrEP is concerning. One explanation may be that doctors in Berlin are targeting information at the individuals they feel will benefit the most from PrEP. This is supported by our finding that those at the highest risk of HIV infection were significantly more likely to name their doctor as a source of information about PrEP than those at low risk.

Targeting information to a small group of MSM might also be a way for doctors in Berlin (and Germany as a whole) to cope with a system of payment for office-based health professionals that often makes it difficult to recover the cost of consultations as lengthy as those needed to educate patients about preventive measures such as PrEP [43,44]. However, one of the goals of PrEP provision is to avoid informal use of the medications. Our study provides some evidence that this targeting, if it is taking place, may be too narrow, leading to unintended negative consequences for individual and public health as detailed above. These concerns are further underscored by our finding that almost one quarter of participants who had no history of PrEP use reported that they had had condomless anal intercourse with more than one partner over the past six months.

The cost of PrEP is described frequently in the literature as a barrier to its use [45–47]. We therefore included a question in our survey to identify whether cost might be seen as a barrier by participants in our sample. However, because the price of a month's supply of generic PrEP in Germany fell from approximately 600 euros to as low as 50 euros during the study period, our data on this question are of limited validity. Regardless, the majority of participants indicated that 50 euros per month was an acceptable price if PrEP continued not to be covered by public health insurance. Interestingly, most participants also felt that PrEP should be covered by public health insurance for all MSM who wanted to use it, regardless of their HIV risk. This suggests that participants may see access to PrEP as a matter of equality in contrast to what may be a narrowly targeted approach among doctors, as discussed above. In fact, almost one third of participants with no history of PrEP use indicated that they would consider using PrEP if a doctor prescribed it for them.

In addition to being more likely to receive information about PrEP from their doctors, participants at higher risk of HIV infection because of multiple CAI partners, or because of multiple CAI partners and an STI diagnosis, were much more likely to express the desire to take PrEP or to have a history of PrEP use than MSM at low risk. This is encouraging, both from an individual and public health perspective, yet it again raises the issue of informal PrEP use. Almost half of our participants stated that they had, or would have, anal sex without a condom more often when taking PrEP, thus increasing their risk of infection with other STIs. Moreover, those who expressed a desire to take PrEP or had a history of PrEP use were significantly more likely than those who did not to report that they did or would engage in CAI. While STIs can be detected and treated early among PrEP users who are well integrated into a regular STI testing scheme, this is rather unlikely for people who obtain PrEP through informal channels or take it irregularly.

We found evidence that MSM with family but not personal origins outside Germany were significantly more likely to have a history of PrEP use than MSM with family origins within Germany. Unfortunately, participants rarely specified which countries their non-German-born parent or parents came from. We therefore cannot draw any conclusions about whether this subgroup is representative of MSM whose families come from the historical source

countries of migration to Berlin, such as Turkey, Poland and Russia [48]. Further studies are necessary to assess whether the needs of ethnic minorities in Berlin and Germany as a whole are being adequately met. The same applies to MSM in lower income groups, who are probably underrepresented in our sample. The state government of Berlin is planning to target this specific group with a model project that should provide free PrEP services to a limited number of financially deprived MSM [37].

Some of our findings are similar to those of an anonymous online survey of MSM conducted in Germany in 2016 [49]. The mean age of participants was the same, awareness of PrEP was similarly common, and similar proportions of participants reported having had an STI diagnosis within the past six months and being more likely not to use a condom when taking PrEP. Furthermore, the proportion of patients in our sample who reported obtaining PrEP only through a private prescription (32.1%) was similar to the proportion of patients in the sample of Spinner et al. [49] who reported accessing PrEP under medical supervision (29.2%). Moreover, the proportion of participants in both studies who reported obtaining at least some of their PrEP through informal channels was similarly high at 60% to 70%.

While sexual risk behaviour was also identified by Spinner et al. as a predictor of having a history of PrEP use, they defined risk contacts as CAI under the influence of recreational drugs, whereas we collected data on the frequency of anal intercourse overall and of CAI. Nevertheless, the similarities suggest that both study samples may be broadly representative of the broader population of MSM in Germany. This being said, the proportion of participants who reported a history of PrEP use in the survey by Spinner et al. [49] (7.5%) was considerably lower than in our sample. This in unsurprising, however, if we consider that PrEP uptake in a city like Berlin with a large population of MSM is likely to be higher than in Germany as a whole. In a survey of MSM in Amsterdam from 2015,[50] the proportion of participants aware of PrEP was much lower than that in our study. However, given the rapid developments in the field of PrEP, such as growing evidence to support its efficacy and safety, efforts to implement PrEP and reductions in price, this difference between data from 2015 and 2017/18 is similarly unsurprising.

This study has important limitations. First, when asking participants about their number of CAI partners, we did not distinguish between insertive and receptive CAI, although the risk of infection clearly differs between the two. However, we were interested primarily in obtaining data that could be grouped and analysed according to the CDC recommendations for PrEP use. Second, like other sampling strategies, facility-based sampling introduces a selection bias that can limit the external validity of findings [51–53]. While a strength of our sample is its broad age range (18–79 years), it likely reflects the part of the MSM community in Berlin that is well integrated within and seeking information from LGBTI counselling centres and HIV-specialist practices. This may help explain the high proportion of university degrees among our participants and the low proportion of participants who reported that they or their parents had been born in the countries with the historically highest flows of migration to Berlin. It is therefore important to consider that our sample may not include MSM in lower income groups or who are facing cultural barriers to access and might have the greatest need for information and, indeed, PrEP services. Moreover, it is likely that some of the participating doctors did not, as they had been asked, invite all eligible patients to take part in the survey. This may have led to patients being more likely to have been included if they asked about PrEP of their own volition and therefore to selection bias. A third important limitation is that, while we did not exclude transgender MSM from participating in the survey, we did not explicitly instruct participating centres to include this group, nor did we measure how many transgender MSM may have taken part. Other sampling strategies would have been necessary to obtain meaningful data on transgender MSM's attitudes towards PrEP but would have gone beyond the scope

of our study. Fourth, although we attempted to recruit several HIV specialist practices in former East Berlin, only one of these chose to participate. It was very centrally located and may not cater to many patients on the eastern outskirts of the city, where there are larger numbers of people with a family history of migration from the former Soviet Union and Vietnam [48]. Obtaining a representative sample of minorities, particularly sexual ones, remains a challenge. Nevertheless, many of the sociodemographic characteristics in our sample are comparable to those among participants in earlier, online surveys of MSM in Germany [49,54]. The mean age of our participants and the proportion of those who reported that they or their parents had been born outside of Germany were similar to the figures recorded by the participating sexual health counselling centres in 2016 as part of their routine data collection (mean age: 34.2 years; 52.2% born themselves or with parents born outside Germany) [55].

Lastly, we could not assess patterns of non-response because we had no information on the total number of patients or clients who were invited to participate in the survey versus the number who declined. However, as is the case for all epidemiological research, the size of the observed associations is important. In our study, the relatively high response rate for this type of research, the multivariable analysis used and the large size of the observed associations, particularly for sexual risk behaviour, suggest that our findings are not likely to result from non-response bias alone.

Our post-estimation regression diagnostics, including tests for multicollinearity and potentially influential observations, as well as sensitivity analyses including all variables of a priori interest, suggest that the findings of both regression models are robust.

Conclusions

Our facility-based survey of almost 500 HIV-negative MSM in Berlin found a very high level of awareness of PrEP but also a strong need for more education on its pros, cons and proper use. From an individual and public health perspective, this need should be regarded as acute given that almost one quarter of our participants who reported never having used PrEP also reported having had condomless anal intercourse with more than one partner in the past six months. Moreover, at least 60% of participants who reported using PrEP had obtained some or all of it through informal channels, making it less likely that they were always taking their medication under medical supervision. We also found evidence that doctors in Berlin might be sensibly targeting the provision of PrEP services at those with the highest risk of HIV infection, but that this targeting could be too narrow, allowing some people to fall through the gaps. If the Berlin state government intends to go beyond its commitments as part of the Fast-Track Cities initiative, policy makers at the state and federal levels will need to consider recent calls from the German STI Association to improve access to PrEP and PrEP education through regular health services.

Supporting information

S1 File. English language questionnaire.
(PDF)

S2 File. German language questionnaire.
(PDF)

S3 File. Minimal underlying data set and codebook. Age of respondents and qualitative data have been removed to ensure patient anonymity.
(XLSX)

Acknowledgments

The authors would like to acknowledge and thank the following people: Dr. med. Dietmar Schranz and Dr. med. Klaus Fischer and staff (Gemeinschaftspraxis Dietmar Schranz und Klaus Fischer); Dr. med. Dorothea Schleehauf and staff (Praxiszentrum Kaiserdamm); Falk Lemanski and other staff (Praxis Wünsche); the staff of Novopraxis Berlin GbR; Anna Müller-Claud and other staff (Praxis Jessen^2 + Kollegen); Dr. med. Jens Olaf Mielcke, Matthias Freiwald, Dr. med. Michael Rausch, Thomas Reineke, Dr. med. Yves Zimmer and staff (Ärztezentrum Nollendorfplatz); and the staff of the following counselling / testing centres: Mann-O-Meter e.V., Pluspunkt Berlin (Schwulenberatung Berlin gGmbH), Fixpunkt e.V., and Berliner AIDS-Hilfe e.V. for their participation in distributing questionnaires and collecting data. The study would not have been possible without the participants who consented to be part of the study. Also, we would like to acknowledge and thank Dr. Jochen Kruppa for providing support with respect to statistical analyses, Dr. Ulrich Marcus from the Robert Koch-Institut for providing demographic data from the participating counselling centres, and Dr. Joseph Pearson for providing advice on the development of the questionnaire.

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Publication 2: Kutscha F, Gaskins M, **Sammons M**, Nast A, Werner RN. HIV Pre-Exposure Prophylaxis (PrEP) Counseling in Germany: Knowledge, Attitudes and Practice in Non-governmental and in Public HIV and STI Testing and Counseling Centers. Frontiers in Public Health. 2020;8(298). doi: 10.3389/fpubh.2020.00298.

I was involved in the development of the questionnaire and study design. I commented on the first draft of the publication and approved the final draft of the manuscript.

Journal Data Filtered By: **Selected JCR Year: 2020** Selected Editions: SCIE Selected Categories: **"PUBLIC, ENVIRONMENTAL and OCCUPATIONAL HEALTH"** Selected Category Scheme: WoS

Gesamtanzahl: 203 Journale

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1	MMWR Surveillance Summaries	3,806	58.769	0.012980
2	MMWR Recommendations and Reports	3,288	55.857	0.011230
3	Lancet Global Health	16,662	26.763	0.051650
4	Annual Review of Public Health	9,927	21.981	0.013560
5	Lancet Public Health	5,793	21.648	0.014840
6	Lancet Planetary Health	2,540	19.173	0.008590
7	MMWR-MORBIDITY AND MORTALITY WEEKLY REPORT	31,127	17.586	0.078080
8	BULLETIN OF THE WORLD HEALTH ORGANIZATION	19,297	9.408	0.015980
9	AMERICAN JOURNAL OF PUBLIC HEALTH	51,398	9.308	0.056870
10	ENVIRONMENTAL HEALTH PERSPECTIVES	48,245	9.031	0.028380
11	JOURNAL OF TRAVEL MEDICINE	5,260	8.490	0.004900
12	EUROPEAN JOURNAL OF EPIDEMIOLOGY	11,622	8.082	0.017840
13	TOBACCO CONTROL	10,279	7.552	0.015380
14	INTERNATIONAL JOURNAL OF EPIDEMIOLOGY	30,944	7.196	0.045590
15	Current Environmental Health Reports	1,967	7.122	0.004720
16	ENVIRONMENTAL RESEARCH	28,576	6.498	0.034260
17	JOURNAL OF CLINICAL EPIDEMIOLOGY	36,224	6.437	0.028360
18	JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH-PART B-CRITICAL REVIEWS	2,226	6.393	0.001410
19	Current Pollution Reports	1,107	6.373	0.001940

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
20	EPIDEMIOLOGIC REVIEWS	3,938	6.222	0.002790
21	Travel Medicine and Infectious Disease	5,034	6.211	0.003430
22	Environmental Health	7,567	5.984	0.009260
23	INTERNATIONAL JOURNAL OF HYGIENE AND ENVIRONMENTAL HEALTH	7,425	5.840	0.008110
24	INDOOR AIR	7,488	5.770	0.005760
25	DRUG SAFETY	6,817	5.606	0.006840
26	Journal of Exposure Science and Environmental Epidemiology	5,227	5.563	0.004500
27	BMJ Global Health	4,992	5.558	0.018060
28	Evolution Medicine and Public Health	758	5.425	0.001860
29	International Journal of Transgenderism	1,381	5.333	0.002130
30	AMERICAN JOURNAL OF PREVENTIVE MEDICINE	28,400	5.043	0.037310
31	SCANDINAVIAN JOURNAL OF WORK ENVIRONMENT & HEALTH	6,700	5.024	0.004530
32	JOURNAL OF ADOLESCENT HEALTH	20,914	5.012	0.024870
33	AMERICAN JOURNAL OF EPIDEMIOLOGY	43,617	4.897	0.031670
34	Antimicrobial Resistance and Infection Control	3,629	4.887	0.008170
35	EPIDEMIOLOGY	16,437	4.822	0.016740
36	Health Reports	1,781	4.796	0.001770
37	Clinical Epidemiology	4,754	4.790	0.010760
38	PALLIATIVE MEDICINE	7,332	4.762	0.009100
39	SOCIAL SCIENCE & MEDICINE	57,968	4.634	0.052130
40	ENVIRONMENTAL GEOCHEMISTRY AND HEALTH	6,557	4.609	0.004550
41	GeoHealth	381	4.529	0.001190

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Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
42	Journal of Global Health	2,764	4.413	0.007500
43	OCCUPATIONAL AND ENVIRONMENTAL MEDICINE	11,253	4.402	0.008990
44	JOURNAL OF RURAL HEALTH	2,866	4.333	0.004050
45	CANCER EPIDEMIOLOGY BIOMARKERS & PREVENTION	23,046	4.254	0.021910
46	NICOTINE & TOBACCO RESEARCH	11,360	4.244	0.016740
47	Globalization and Health	3,266	4.185	0.015780
48	LGBT Health	1,684	4.151	0.005290
49	QUALITY OF LIFE RESEARCH	19,584	4.147	0.017860
50	JMIR Serious Games	641	4.143	0.000970
51	JMIR Public Health and Surveillance	2,430	4.112	0.005860
52	HEALTH & PLACE	9,762	4.078	0.010030
53	PUBLIC HEALTH NUTRITION	18,093	4.022	0.019490
54	PREVENTIVE MEDICINE	20,705	4.018	0.028980
55	PAEDIATRIC AND PERINATAL EPIDEMIOLOGY	4,004	3.980	0.004310
56	JOURNAL OF HOSPITAL INFECTION	12,760	3.926	0.011240
57	International Journal of Health Geographics	3,384	3.918	0.002450
58	One Health	829	3.800	0.001560
59	ANNALS OF EPIDEMIOLOGY	8,616	3.797	0.011210
60	Journal of Infection and Public Health	3,870	3.718	0.006030
61	JOURNAL OF EPIDEMIOLOGY AND COMMUNITY HEALTH	18,466	3.710	0.015600
62	Frontiers in Public Health	8,172	3.709	0.017640
63	Environmental Health and Preventive Medicine	2,240	3.674	0.002340

Selected JCR Year: 2020; Selected Categories: "PUBLIC, ENVIRONMENTAL and OCCUPATIONAL HEALTH"

frontiers in Public Health

ORIGINAL RESEARCH
published: 14 July 2020
doi: 10.3389/fpubh.2020.00298

HIV Pre-Exposure Prophylaxis (PrEP) Counseling in Germany: Knowledge, Attitudes and Practice in Non-governmental and in Public HIV and STI Testing and Counseling Centers

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OPEN ACCESS

Edited by:
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Specialty section:
This article was submitted to Infectious Diseases - Surveillance, Prevention and Treatment, a section of the journal Frontiers in Public Health

Received: 20 January 2020
Accepted: 04 June 2020
Published: 14 July 2020

Citation:
Kutscha F, Gaskins M, Sammons M, Nast A and Werner RN (2020) HIV Pre-Exposure Prophylaxis (PrEP) Counseling in Germany: Knowledge, Attitudes and Practice in Non-governmental and in Public HIV and STI Testing and Counseling Centers. Front. Public Health 8:298. doi: 10.3389/fpubh.2020.00298

Background: Providers of sexual health services play an important role in counseling persons at risk of acquiring HIV. The aim of the present study was to investigate the knowledge of and attitudes toward HIV pre-exposure prophylaxis (PrEP) among counselors in non-governmental counseling centers ("NG counseling centers") and in counseling centers of the local health authorities ("local health offices") in Germany and to determine the extent to which PrEP plays a role in their current counseling practice.

Methods: An anonymous cross-sectional study using an online questionnaire was conducted among counselors from sexual health centers across Germany. All NG counseling centers in Germany offering HIV testing were asked to participate. For each NG counseling center, a local health office in the same city was also invited. A "knowledge score" and an "attitudes score" were calculated from single items on various relevant aspects. The association of these scores with the proportion of PrEP advice provided proactively in sessions with men who have sex with men (MSM) and trans persons who met the German and Austrian guideline criteria for being offered PrEP ('at-risk clients') was quantified.

Results: From Oct. to Dec. 2018, 145 counselors completed the survey. Both self-assessed knowledge of PrEP and attitudes toward PrEP were greater or more positive among counselors from NG counseling centers compared with counselors from local health offices [*Median* knowledge score (range 0-20): 18.0 (*IQR* = 5.0) vs. 14.0 (*IQR* = 4.0), $p<0.001$; *median* attitudes score (range 0-20): 18.0 (*IQR* = 4.0) vs. 14.0 (*IQR* = 6.8), $p<0.001$]. The proportion of PrEP advice provided proactively in sessions with at-risk clients was larger in counseling centers than in local health offices [50.0% (*IQR* = 60.0) vs. 30.0% (*IQR* = 70.0); $p = 0.003$]. The results of the multiple linear regression model indicate that knowledge and attitudes of the individual counselors,

but not the type of center in which they worked, were independent predictors of the proportion of proactive advice on PrEP.

Conclusions: There is room for improvement in the current PrEP counseling practice of sexual health services in Germany. The findings of the present study suggest opportunities to improve the implementation of PrEP as part of a comprehensive HIV prevention strategy.

Keywords: HIV pre-exposure prophylaxis, PrEP, counseling, public health, HIV prevention, health services research

INTRODUCTION

In 2018, an estimated 2,400 new infections with HIV, primarily in men who have sex with men (MSM), occurred in Germany (1) and the prevention of HIV remains a major public health concern (2). Public health strategies to prevent sexually transmitted HIV infection have traditionally focused on behavioral interventions such as supporting condom use in sexually active populations. However, apart from the effects of early diagnosis and treatment of HIV infections, the latter of which is highly effective at preventing the transmission of HIV (3–5), a relatively new form of biomedical HIV prevention, namely HIV pre-exposure prophylaxis (PrEP), and its broad implementation in populations at risk has likely contributed to declining HIV incidence rates in some major cities such as San Francisco, London, and Sydney (6–8). The efficacy and safety of PrEP in MSM and trans persons has been shown in various randomized controlled studies (9–13) and cohort studies (14–17). International and national guidelines recommend the use of PrEP for HIV-negative people at substantial risk of acquiring HIV (18–20). According to the German and Austrian guideline published in May 2018, PrEP should be offered to HIV-negative adult MSM and trans persons who had a sexually transmitted infection (STI) in the past 12 months or who report having had and/or having the intent to practice condom-less anal sex (19). The cost of PrEP has been covered by the public health insurance in Germany only since September 2019.

In the US, the uptake of PrEP has been influenced largely by different, primarily socioeconomic and individual information-related factors (21–27). For the German context, few data on PrEP use are available. A survey among MSM in Berlin identified a substantial gap between the indication to use PrEP and actual PrEP use: almost a quarter of the non-PrEP-using participants reported sexual behavior that put them at risk of acquiring HIV (28). Results from a survey among users of a dating platform for MSM in 2018 suggest that PrEP use among MSM in Germany is less common compared with some other western European countries (29). Access to information about PrEP has been shown to be an important barrier to the initiation of PrEP (28). However, surveys from the US suggest that knowledge of PrEP may also be limited among physicians (30, 31). A survey among Dutch providers of STI and HIV services showed a moderate willingness to prescribe PrEP and limited knowledge of PrEP, especially among STI specialists (32). The provision of PrEP-related training for physicians has been discussed as a factor that could improve the implementation of PrEP (30, 31).

In Germany, HIV testing and counseling on HIV prevention is provided primarily by specialist physicians working in office-based practices and by sexual health services such as HIV and STI testing and counseling centers. The latter are either non-governmental, community-based counseling centers ("NG counseling centers") or public sexual health services of the local health authorities ("local health offices"). Both types of counseling centers offer low-threshold, anonymous HIV and STI testing and counseling and play an important role in the dissemination of information on HIV and strategies to prevent infections (2, 33). To date, no data have been available on PrEP-related counseling competence, knowledge, and attitudes among counselors working at either type of organization.

With the present study, we aimed to investigate the extent to which PrEP plays a role in the counselors' counseling practice, as well as the factors influencing the proportion of proactive PrEP advice they provide to clients at risk of sexually acquired HIV. Furthermore, the relevance of different barriers for potential PrEP users to initiate PrEP as perceived by the counselors was evaluated. With this knowledge we aimed to identify barriers to and facilitators of PrEP implementation and opportunities to improve PrEP implementation among MSM and trans persons in Germany. This study comprised part of the master's thesis of the first author (FK).

METHODS

Study Design

For this cross-sectional study, an online survey was conducted among counselors working in non-governmental, community-based counseling centers ("NG counseling centers") or in counseling centers of the local health authorities ("local health offices"). The anonymous, self-administered questionnaire was available online from October to December 2018. The study protocol was approved by the local ethics committee of Charité – Universitätsmedizin Berlin (EA1/006/19) and informed consent was obtained from all participants.

Setting and Eligibility

Counselors from NG counseling centers and local health offices were eligible to participate if they worked in the field of counseling clients on HIV and other STIs, regardless of their primary professional qualification. All NG counseling centers offering HIV testing and counseling listed by the comprehensive, publicly available register provided by "HIV and more" (34) were asked to participate. In order to ensure the comparability of

TABLE 1 | Dimensions and their operationalisation used to assess **(A)** knowledge and counseling competence and **(B)** attitudes toward PrEP.

Dimension		**Operationalisation and scores**				
Do you agree or disagree with the following statements?		***Strongly disagree***	***Disagree***	***Neither agree nor disagree***	***Agree***	***Strongly agree***
(A) Knowledge and counseling competence						
Global assessment	"I am well-informed about PrEP"	0	1	2	3	4
Indications	"I am able to comprehensively give clients advice on whether it makes sense to take PrEP in their respective case"	0	1	2	3	4
Adverse effects	"I am able to comprehensively give clients advice on the adverse effects of PrEP"	0	1	2	3	4
Modalities of intake	"I am able to comprehensively give clients advice on the possible modalities of intake of PrEP (e.g., continuous vs. on-demand)"	0	1	2	3	4
Investigations	"I am able to comprehensively give clients advice on the medical investigations necessary during the use of PrEP"	0	1	2	3	4
'Knowledge score'		Summative score with values ranging from 0 to 20				
(B) Attitudes toward PrEP						
Global assessment	"I think that PrEP is an important element of HIV prevention strategies"	0	1	2	3	4
Reliability	"I think that PrEP is a reliable method to protect oneself from HIV"	0	1	2	3	4
Adverse effects	"I think that PrEP is a method to protect oneself from HIV that has few side effects"	0	1	2	3	4
Availability of better alternatives	"I think that PrEP is unnecessary, because there are better alternatives to protect oneself from HIV"	4	3	2	1	0
Reimbursement of costs	"I think that PrEP should be paid for by the statutory health insurance"	0	1	2	3	4
'Attitudes score'		Summative score with values ranging from 0 to 20				

NG counseling centers with the participating local health offices, a local health office in the same or in a comparable city was invited for each NG counseling center. The selected centers were contacted by email and requested to forward the survey invitation to all eligible counselors within their organization. A reminder email was sent three to four weeks after the initial invitation. Additionally, all centers were contacted by telephone to enhance the participation rate. This telephone call also served to obtain information on the number of counselors to whom the invitation email had been forwarded in each organization.

Questionnaire and Variables

A standardized German-language questionnaire exploring knowledge of and attitudes toward PrEP among counselors and their counseling practice on PrEP is not available; the questionnaire was therefore developed for the purpose of the present study. The original draft questionnaire (FK) was tested and discussed (RW, MG, MS, AN) to identify and correct errors concerning spelling, expression and grammar as well as problems concerning the comprehensibility of the content and design. The questionnaire covered the following topics:

- Socio-demographic data and information about the type of center
- Counseling sessions and counseling practice regarding PrEP
- Self-assessed PrEP-related knowledge and self-reported attitudes
- Need for information or training materials to improve PrEP counseling
- Perceived barriers for potential users to initiate PrEP.

After providing informed consent and answering the initial question on the type of center (NG counseling center vs. local health office), participants could, if they so desired, leave any number of questions unanswered. The participants were provided with a brief summary on the efficacy and safety of PrEP, and with information about the recommendations of the German and Austrian guideline on the indications for offering PrEP.

Socio-demographic data comprised gender, age, primary professional qualification and work experience in counseling on sexual health issues. Furthermore, contextual information on the counseling center was obtained, including which of the 16 states in Germany the organization was located and size of the city, the number of HIV tests provided per month and the number of these that were positive. In addition, the total number of personal counseling sessions with MSM and trans persons per month and the number of sessions with MSM and trans persons who met the criteria to be counseled on PrEP according to the German and Austrian guideline ("at-risk clients"), was obtained. Regarding counseling practice, participants were asked to indicate the proportion of counseling sessions with these at-risk-clients (a) in which the topic PrEP had been addressed by the clients themselves and (b) in which the counselors themselves had proactively addressed the topic.

PrEP-related knowledge and counseling competence and the attitudes toward PrEP were quantified using a self-assessment in terms of agreement with statements about various aspects relevant in this context (**Table 1**). Fully verbalized bipolar

five-step Likert scales with an ambivalent scale center were provided to quantify the agreement with these statements. The items were presented randomly to each participant in a different order. Since the evaluation of individual Likert-scaled variables is considered less reliable compared to a summative multi-item scale (35), a summative "knowledge score" and "attitudes score" were calculated from the five individual knowledge and attitudes variables. The total scores assume values between 0 and 20, with high values representing good knowledge and counseling competence, or positive attitudes toward PrEP, respectively.

Furthermore, the participants were asked whether training was offered and whether inhouse guidelines or standard operating procedures on PrEP counseling were available in their organization. In addition, participants could indicate whether they wished to receive training or information material on PrEP counseling. A multiple-choice list was offered to assess tools or training that could be helpful to improve their counseling work or enhance practicability. To assess potential barriers to PrEP initiation, various aspects were presented, and participants were asked to rate the relevance of these potential barriers on an eleven-level, end-verbalized rating scale with numeric markers (0 = no relevance to 10 = highest relevance) according to their counseling experience. Again, the items were presented to each participant in randomized order.

Sample Size and Statistical Methods

Since the questionnaire was expressly designed for the purpose of this study, no data on expected means and variability were available. The aim was to include all NG counseling centers offering HIV testing and a corresponding number of matched local health offices. Therefore, no sample size calculation was performed. Statistical analyses were conducted with IBM® SPSS® Statistics version 25 (sample characteristics and bivariate statistics) and with STATA SE version 14.2 (multiple linear regression). To describe the sample characteristics and the results, descriptive statistics were used depending on the data quality. The internal consistency of the summative knowledge and attitudes scores was quantified with Crohnbach's alpha. To quantify associations between variables, independent samples *t*-tests, the Mann-Whitney *U* test and Pearson's Chi squared tests were used, depending on the data quality. A multiple linear regression, using the backward elimination method, was modeled to identify predictors of the proportion of proactive advice on PrEP in sessions with at-risk clients. The following variables for this regression model were purposefully selected a priori: type of center (NG counseling center vs. local health office), gender and years of practical work experience of the participant, size of the city, rate of positive HIV tests, knowledge score, and attitudes score. The stopping rule for the elimination of individual variables in the multiple linear regression was $p < 0.2$. Variance inflation factor (VIF) statistics and condition number were used to verify that there was no multi-collinearity of the predictors and instability of the regression coefficients, respectively. Missing cases were excluded in a listwise fashion. The level for statistical significance was set at $p = 0.05$.

RESULTS

Recruitment, Participation, and Response Rate

The letter of invitation to participate in the survey was sent to a total of 76 centers (38 NG counseling centers and 38 local health offices). Overall, 179 counselors opened the survey and began to fill it in. Of these, 145 provided information on the type of counseling center at which they worked (NG vs. local health office), which was the initial and only compulsory questionnaire item. Thus, the sample size was 145, of which 56 indicated working in a local health center and 89 in an NG counseling center. The number of counselors to whom the invitation was forwarded within each invited center could be obtained from phone calls with 62 centers and was $M = 2.96$ ($SD = 2.56$) in local health offices and $M = 5.58$ ($SD = 5.07$) in NG counseling centers. Five of the selected local health offices did not participate in the survey. Based on this information, the estimated number of counselors invited to participate in the survey was 98 for local health offices and 212 for NG counseling centers. Using these estimates, the response rate was 57.1% for local health offices and 42.0% for NG counseling centers. Of the 145 participants, 77.9% completed the questionnaire in its entirety.

Demographic Data

Demographic data of the sample are shown in **Table 2**. The mean age of the participants was 46.0 years ($SD = 11.7$). 76 participants (52.4%) defined themselves as male, 61 (42.1%) as female, and two (1.4%) as gender non-binary. The majority ($n = 93$, 64.1%) indicated that their primary professional qualification was social work; a further 15 (10.3%) indicated that they were physicians, 14 (9.7%) that they were psychologists and four (2.8%) that they were nursing professionals. A large majority of the participants indicated that their counseling center was located in a large city with more than 100,000 inhabitants ($n = 89$, 61.4%) or in a major city with more than 1,000,000 inhabitants ($n = 43$, 29.7%). The vast majority ($n = 123$, 84.8%) indicated that their organization was located in one of the old German states (western Germany) or the city state of Berlin. Statistically significant associations between type of center and demographic data were seen for gender ($\chi^2_{(df = 2,\ n = 139)} = 17{,}40$, $p < 0.001$) and primary professional qualification ($\chi^2_{(df=4, n = 139)} = 19{,}85$, $p = 0.001$), see **Table 2**.

Counseling Sessions and Practice

Table 3 depicts data on the number of counseling sessions and HIV tests reported by the participants. Counselors averaged 36.6 counseling sessions with MSM and trans persons per month ($SD = 48.2$) and 16.0 sessions with MSM and trans persons who met the criteria to be offered PrEP according to the recommendations of the German and Austrian guideline on PrEP (at-risk clients) ($SD = 22.2$). No significant differences were seen with regard to these two variables between NG counseling centers and local health offices. However, counselors from local health offices reported a higher number of HIV tests per month ($Mdn = 180$, $IQR = 190$) than did participants from NG counseling centers ($Mdn = 47.5$, $IQR = 73.8$), $U = 1103.5$,

TABLE 2 | Demographic data and contextual characteristics of the sample.

Variable	Total sample		Type of center				
			Local health offices		NG counseling centers		
N	145		56		89		
Age in years (*n* = 139)							$p = 0.679^{\dagger}$
Mdn (*IQR*)	48.00	(19.00)	48.00	(17.00)	47.50	(21.75)	
M (*SD*)	46.03	(11.67)	46.51	(11.51)	45.75	(11.82)	
Min; *Max*	19-67	19-62	23-67				
Gender (*n*, %)							$p < 0.001^{\S}$
Female	61	(42.1%)	34	(60.7%)	27	(30.3%)	
Male	76	(52.4%)	17	(30.4%)	59	(66.3%)	
Non-binary	2	(1.4%)	0	(0%)	2	(2.2%)	
Not specified	6	(4.1%)	5	(8.9%)	1	(1.1%)	
Professional qualification (*n*, %)							$p = 0.001^{\S}$
Social work	93	(64.1%)	37	(66.1%)	56	(62.9%)	
Psychology	14	(9.7%)	2	(3.6%)	12	(13.5%)	
Nursing	4	(2.8%)	1	(1.8%)	3	(3.4%)	
Physician	15	(10.3%)	11	(19.6%)	4	(4.5%)	
Other	13	(9.0%)	0	(0%)	13	(14.6%)	
Not specified	6	(4.1%)	5	(8.9%)	1	(1.1%)	
Size of the location (*n*, %)							$p = 0.138^{\S}$
Major city (>1,000,000)	43	(29.7%)	15	(26.8%)	28	(31.5%)	
Large city (>100,000)	89	(61.4%)	31	(55.4%)	58	(65.2%)	
City (>10,000)	7	(4.8%)	5	(8.9%)	2	(2.2%)	
Small city (≤ 10,000)	1	(0.7%)	1	(1.8%)	0	(0%)	
Not specified	5	(3.4%)	4	(7.1%)	1	(1.1%)	
Federal state (*n*, %)							$p = 0.072^{\S}$
Baden-Wuerttemberg	20	(13.8%)	3	(5.4%)	17	(19.1%)	
Bavaria	22	(15.2%)	8	(14.3%)	14	(15.7%)	
Berlin	15	(10.3%)	7	(12.5%)	8	(9.0%)	
Brandenburg	9	(6.2%)	3	(5.4%)	6	(6.7%)	
Bremen	1	(0.7%)	0	(0%)	1	(1.1%)	
Hamburg	13	(9.0%)	4	(7.1%)	9	(10.1%)	
Hesse	12	(8.3%)	2	(3.6%)	10	(11.2%)	
Mecklenburg-Western Pomerania	2	(1.4%)	2	(3.6%)	0	(0%)	
Lower Saxony	8	(5.5%)	6	(10.7%)	2	(2.2%)	
North Rhine-Westphalia	22	(15.2%)	8	(14.3%)	14	(15.7%)	
Rheinland-Pfalz	0	(0%)	0	(0%)	0	(0%)	
Saarland	4	(2.8%)	3	(5.4%)	1	(1.1%)	
Saxony	0	(0%)	0	(0%)	0	(0%)	
Saxony-Anhalt	1	(0.7%)	0	(0%)	1	(1.1%)	
Schleswig-Holstein	6	(4.1%)	3	(5.4%)	3	(3.4%)	
Thuringia	0	(0%)	0	(0%)	0	(0%)	
Not specified	10	(6.9%)	7	(12.5%)	3	(3.4%)	
Professional experience in years (n = 138)							$p = 0.838^{\dagger}$
Mdn (*IQR*)	11.50	(18.25)	11.00	(17.50)	12.00	(19.75)	
M (*SD*)	14.19	(10.38)	14.14	(10.02)	14.23	(10.63)	
Min; *Max*	0.5-40		0.5-31		1-40		

IQR, inter quartile range; M, mean; Max, maximum; Mdn, median; Min, minimum; SD, standard deviation. †*From Mann-Whitney U tests of the null hypothesis that the median value of participants from local health offices is equal to that of participants from NG counseling centers.* §*From Pearson's Chi squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, by type of counseling center.*

TABLE 3 | Counseling sessions and HIV-tests.

Variable	Total sample		Type of center				
			Local health office		NG counseling center		
Number of overall counseling sessions with MSM and trans persons per month (n = 126)							$p = 0.784^{\dagger}$
Mdn (*IQR*)	20.00	(35.00)	20.00	(40.00)	25.00	(30.00)	
M (*SD*)	36.55	(48.23)	39.21	(52.13)	34.96	(46.03)	
Min; *Max*	0-330		0-270		0-330		
Number of sessions with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guideline (at-risk clients) (n = 116)							$p = 0.780^{\dagger}$
Mdn (*IQR*)	10.00	(10.00)	10.00	(12.50)	10.00	(10.00)	
M (*SD*)	15.97	(22.17)	15.38	(18.70)	16.35	(24.23)	
Min; *Max*	0-170		0-80		1-170		
Overall number of HIV tests per month (n = 123)							$p < 0.001^{\dagger}$
Mdn (*IQR*)	60.00	(175.00)	180.00	(190.00)	47.50	(73.75)	
M (*SD*)	112.69	(109.85)	162.81	(116.12)	81.70	(93.87)	
Min; *Max*	3-400		3-400		8-350		
Number of positive HIV test results per month (n = 117)							$p = 0.311^{\dagger}$
Mdn (*IQR*)	0.00	(1.00)	1.00	(1.00)	0.00	(1.00)	
M (*SD*)	0.67	(0.83)	0.78	(0.90)	0.60	(0.78)	
Min; *Max*	0-4		0-3		0-4		
Proportion of positive HIV test results among overall number of HIV tests (n = 117)							$p = 0.373^{\dagger}$
Mdn (*IQR*)	0.00%	(0.93)	0.33%	(0.65)	0.00%	(1.67)	
M (*SD*)	0.74%	(1.49)	0.34%	(0.38)	0.99%	(1.84)	
Min; *Max*	0-12.5%		0-1.25%		0-12.5%		

IQR, inter quartile range; M, mean; Max, maximum; Mdn, median; Min, minimum; SD, standard deviation. † *From Mann-Whitney U tests of the null hypothesis that the median value of participants from local health offices is equal to that of participants from NG counseling centers.*

$p < 0.001$. No significant differences between the two types of centers were seen with respect to the absolute or the relative number of positive HIV tests per month.

Taking into account the entire sample, the participating counselors indicated on average that in 26.1% of counseling sessions with at-risk clients, the clients themselves had addressed the topic of PrEP ($SD = 22.0$). The proportion of PrEP advice provided proactively by the counselors was indicated to be 52.0% on average ($SD = 34.2$). The proportion of clients addressing the topic of PrEP themselves was larger in NG counseling centers ($Mdn = 30.0\%$, $IQR = 40.0$) than in local health offices ($Mdn = 10.0\%$, $IQR = 10.0$), $U = 877.0$, $p < 0.001$. Similarly, the proportion of PrEP advice provided proactively by the counselors was larger in NG counseling centers ($Mdn = 50.0\%$, $IQR = 60.0$) than in local health offices ($Mdn = 30.0\%$, $IQR = 70.0$), $U = 1082.0$, $p = 0.003$. The data are shown in **Table 4**.

Self-Assessment of Knowledge and Counseling Competence

For each of the self-assessed dimensions of knowledge and counseling competence, agreement (and hence a positive self-assessment of knowledge and counseling skills regarding PrEP) was more frequent than indifference or disagreement with the respective statements. However, there was a statistically significant association between the type of center and the agreement for each of the aspects assessed (**Table 5**). For the summative "knowledge score," Crohnbach's alpha was $\alpha = 0.966$. The knowledge score was significantly higher for counselors from NG counseling centers ($Mdn = 18.0$, $IQR = 5.0$) than for counselors from local health offices ($Mdn = 14.0$, $IQR = 4.0$), $U = 679.5$, $p < 0.001$.

Attitudes Toward PrEP

As with the knowledge and counseling competence aspects presented above, agreement with the dimensions assessed for attitudes toward PrEP was more frequent than indifference or disagreement with the four statements expressing positive attitudes toward PrEP. For the statement expressing a negative attitude, disagreement was more frequent than indifference or agreement. Again, for each of the aspects assessed, significant associations between the type of center and agreement were found (**Table 6**). For the summative "attitudes score," Crohnbach's alpha was $\alpha = 0.847$. The attitudes score was significantly higher for counselors from NG counseling centers ($Mdn = 18.0$, $IQR = 4.0$) than for counselors from local health offices ($Mdn = 14.0$, $IQR = 6.8$), $U = 638.5$, $p < 0.001$.

Multiple Linear Regression on the Proportion of Proactive PrEP Advice

A multiple linear regression was modeled to predict the proportion of PrEP advice provided proactively by the counselors to at-risk clients. Applying backward elimination with $p < 0.2$ as

TABLE 4 | Counseling practice in counseling sessions with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guideline (at-risk clients).

Variable	Total sample		Type of center				
			Local health office		NG counseling center		
Proportion of sessions with 'at-risk' MSM and trans persons in which the topic PrEP is addressed by the clients themselves (n = 115)							$p < 0.001^{\dagger}$
Mdn (*IQR*)	20.00%	(30.00)	10.00%	(10.00)	30.00%	(40.00)	
M (*SD*)	26.09%	(21.95)	16.36%	(15.86)	32.11%	(23.11)	
Min; *Max*	0-100%		0-80%		0-100%		
Proportion of sessions with 'at-risk' MSM and trans persons in which the counselors themselves proactively address the topic PrEP (n = 116)							$p = 0.003^{\dagger}$
Mdn (*IQR*)	50.00%	(70.00)	30.00%	(70.00)	50.00%	(60.00)	
M (*SD*)	51.98%	(34.24)	41.33%	(36.72)	58.73%	(30.98)	
Min; *Max*	0-100%		0-100%		10-100%		

IQR, inter quartile range; M, mean; Max, maximum; Mdn, median; Min, minimum; SD, standard deviation. †*From Mann-Whitney U tests of the null hypothesis that the median value of participants from local health offices is equal to that of participants from NG counseling centers.*

a stopping rule for the exclusion of each variable, a significant regression equation was found ($F_{(2,109)} = 10.50$, $p < 0.001$, $n = 112$), with $R^2 = 0.162$ (**Table 7**). The only independent predictors that remained in the model were the knowledge and the attitudes score. Participants' predicted proportion of proactive PrEP advice in sessions with at-risk clients was equal to$-8.208 + 1.692$ (knowledge score) $+ 2.111$ (attitudes score), where knowledge score and attitudes score are coded on scales from 0 to 20 points, with higher scores indicating a more positive self-assessment of knowledge about PrEP and more positive attitudes toward PrEP, respectively, and the proportion of proactive advice on PrEP is coded on a scale from 0 to 100%. The proportion of proactive PrEP advice provided to at-risk clients increased by 1.7% and by 2.1% for each point increase on the knowledge score and on the attitudes score scales, respectively.

Guidelines, Training and Educational Material

Slightly fewer than half of the participants (48.7%, $n = 55$) indicated that their respective organization had in-house PrEP guidelines or standard operating procedures, but a large majority indicated that training on PrEP advice had been offered to them (86.0%, $n = 98$). Fewer than half of the participants indicated that they wished to receive further training on PrEP counseling (44.6%, $n = 50$). Counselors from NG counseling centers indicated having been offered training on PrEP advice more frequently (90.0%, $n = 63$) than counselors from local health offices (79.5%, $n = 35$), but this difference was not statistically significant ($\chi^2_{(df=1,n=114)} = 2{,}447$, $p = 0.118$). Regarding the availability of in-house guidelines and the wish for further training on PrEP no significant differences by type of center were seen, likewise. Asked which of the listed information materials or trainings would improve their counseling practice, decision aids for the clients that present information on PrEP in client-friendly language and in different languages were chosen most frequently (both 78.8%, $n = 89$), followed by a clinical practice guideline that provides a good overview of indications, contraindications and necessary investigations (74.3%, $n = 84$). Less frequently mentioned materials or training were: an app- or SMS-based reminder for PrEP users to promote adherence (58.4%, $n = 66$), information and training for counselors on the management of PrEP (45.1%, $n = 51$), information and training for counselors on the identification of PrEP candidates (38.1%, $n = 43$), and information and training for counselors on talking with clients about sexuality (28.3%, $n = 32$).

Asked to rate the relevance of barriers for potential users to initiate PrEP as perceived in their personal counseling practice, participants pointed to worries about getting infected with other sexually transmitted infections ($M = 5.56$, $SD = 2.73$), the monthly cost of the PrEP medication ($M = 5.33$, $SD = 2.61$), and a lack of information about PrEP in the native language of the client ($M = 5.10$, $SD = 3.33$). Further results on perceived barriers to initiate PrEP are shown in **Table 8**.

DISCUSSION

This is the first survey to assess knowledge, attitudes and counseling practice regarding PrEP among counselors from HIV and STI testing and counseling centers in Germany. Given that targeted counseling of persons at increased risk of acquiring HIV can help them take an informed decision about their personal HIV prevention strategy, counseling centers can play a key role in improving the implementation of PrEP. Providing persons at risk of HIV infection with reliable information on PrEP is an essential prerequisite for improving PrEP implementation in Germany. For this study, we focused on MSM and trans persons who met the criteria to be offered PrEP according to the guideline currently applicable in Germany, and the proportion of PrEP advice proactively provided to this group was one of the key outcomes evaluated within our study.

Regardless of whether they were employed in NG counseling centers or local health offices, participants in the survey indicated that they indeed had counseling sessions with these "at-risk clients" and that they proactively provided PrEP advice in sessions with this group of clients, albeit to varying degrees. The majority of the participating counselors had a positive self-assessment of their knowledge and counseling skills as well as

TABLE 5 | Self-assessment of knowledge and counseling competence.

Variable	Total sample		Type of center				
			Local health office		NG counseling center		
Global assessment: "I am well-informed about PrEP" (*n*, %), *n* = 113							$p < 0.001^{\S}$
Strongly disagree	1	(0.9%)	0	(0.0%)	1	(1.4%)	
Disagree	2	(1.8%)	1	(2.3%)	1	(1.4%)	
Neither agree nor disagree	13	(11.5%)	11	(25.0%)	2	(2.9%)	
Agree	44	(38.9%)	21	(47.7%)	23	(33.3%)	
Strongly agree	53	(46.9%)	11	(25.0%)	42	(60.9%)	
Indications: "I am able to comprehensively give clients advice on whether it makes sense to take PrEP in their respective case" (*n*, %), *n* = 113							$p < 0.001^{\S}$
Strongly disagree	1	(0.9%)	0	(0.0%)	1	(1.4%)	
Disagree	6	(5.3%)	5	(11.6%)	1	(1.4%)	
Neither agree nor disagree	9	(8.0%)	5	(11.6%)	4	(5.7%)	
Agree	38	(33.6%)	22	(51,2%)	16	(22.9%)	
Strongly agree	59	(52.2%)	11	(25.6%)	48	(68.6%)	
Adverse effects: "I am able to comprehensively give clients advice on the adverse effects of PrEP" (*n*, %), *n* = 113							$p < 0.001^{\S}$
Strongly disagree	3	(2.7%)	2	(4.7%)	1	(1.4%)	
Disagree	11	(9.7%)	8	(18.6%)	3	(4.3%)	
Neither agree nor disagree	26	(23.0%)	16	(37.2%)	10	(14.3%)	
Agree	37	(32.7%)	11	(25.6%)	26	(37.1%)	
Strongly agree	36	(31.9%)	6	(14.0%)	30	(42.9%)	
Modalities of intake: "I am able to comprehensively give clients advice on the possible modalities of intake of PrEP (e.g., continuous vs. on-demand)" (*n*, %), *n* = 113							$p < 0.001^{\S}$
Strongly disagree	2	(1.8%)	1	(2.3%)	1	(1.4%)	
Disagree	13	(11.5%)	11	(25.6%)	2	(2.9%)	
Neither agree nor disagree	8	(7.1%)	3	(7.0%)	5	(7.1%)	
Agree	35	(31.0%)	20	(46.5%)	15	(21.4%)	
Strongly agree	55	(48.7%)	8	(18.6%)	47	(67.1%)	
Investigations: "I am able to comprehensively give clients advice on the medical investigations necessary during the use of PrEP" (*n*, %), *n* = 113							$p = 0.002^{\S}$
Strongly disagree	3	(2.7%)	2	(4.7%)	1	(1.4%)	
Disagree	10	(8.8%)	8	(18.6%)	2	(2.9%)	
Neither agree nor disagree	10	(8.8%)	4	(9.3%)	6	(8.6%)	
Agree	37	(32.7%)	18	(41.9%)	19	(27.1%)	
Strongly agree	53	(46.9%)	11	(25.6%)	42	(60.0%)	
Knowledge score (0-20), *n* = 112							$p < 0.001^{\dagger}$
Mdn (*IQR*)	17.00	(6.00)	14.00	(4.00)	18.00	(5.00)	
M (*SD*)	15.64	(4.43)	13.30	(4.38)	17.10	(3.82)	
Min; *Max*	0-20		4-20		0-20		

IQR, inter quartile range; M, mean; Max, maximum; Mdn, median; Min, minimum; SD, standard deviation. †*From Mann-Whitney U tests of the null hypothesis that the median value of participants from local health offices is equal to that of participants from NG counseling centers.* §*From Pearson's Chi squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, by type of counseling center.*

positive attitudes toward PrEP. However, significant differences were found between counselors from NG counseling centers and local health offices: the self-assessment indicated that the former had greater knowledge and counseling skills and more positive attitudes toward PrEP. Furthermore, the proportion of PrEP advice provided proactively in sessions with at-risk clients was larger among counselors from NG counseling centers than among counselors from local health offices.

The differences found between NG counseling centers and local health offices may be attributable to a different basic orientation and organizational policy: whereas NG counseling centers arose from community-based self-help organizations, the local health offices have long focused on advice on HIV and STIs for the overall population and selected risk groups such as sex workers. Whereas the majority of clients in NG counseling centers are MSM (36), this client group only constitutes a minority of the clients in local health offices (37). In the multiple linear regression, however, knowledge of and attitudes toward PrEP remained the only independent predictive factors for the proportion of PrEP advice provided proactively in sessions with

TABLE 6 | Attitudes toward PrEP.

Variable	Total sample		Type of center				
			Local health office		NG counseling center		
Global assessment: "I think that PrEP is an important element of HIV prevention strategies" (*n*, %), *n* = 114							$p < 0.001^{\S}$
Strongly disagree	1	(0.9%)	1	(2.3%)	0	(0.0%)	
Disagree	2	(1.8%)	2	(4.5%)	0	(0.0%)	
Neither agree nor disagree	11	(9.6%)	8	(18.2%)	3	(4.3%)	
Agree	16	(14.0%)	13	(29.5%)	3	(4.3%)	
Strongly agree	84	(73.7%)	20	(45.5%)	64	(91.4%)	
Reliability: "I think that PrEP is a reliable method to protect oneself from HIV" (*n*, %), *n* = 114							$p = 0.003^{\S}$
Strongly disagree	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Disagree	6	(5.3%)	4	(9.1%)	2	(2.9%)	
Neither agree nor disagree	7	(6.1%)	5	(11.4%)	2	(2.9%)	
Agree	33	(28.9%)	18	(40.9%)	15	(21.4%)	
Strongly agree	68	(59.6%)	17	(38.6%)	51	(72.9%)	
Adverse effects: "I think that PrEP is a method to protect oneself from HIV that has few side effects" (*n*, %), *n* = 114							$p = 0.002^{\S}$
Strongly disagree	8	(7.0%)	3	(6.8%)	5	(7.1%)	
Disagree	12	(10.5%)	8	(18.2%)	4	(5.7%)	
Neither agree nor disagree	32	(28.1%)	18	(40.9%)	14	(20.0%)	
Agree	32	(28.1%)	11	(25.0%)	21	(30.0%)	
Strongly agree	30	(26.3%)	4	(9.1%)	26	(37.1%)	
Availability of better alternatives: "I think that PrEP is unnecessary, because there are better alternatives to protect oneself from HIV" (*n*, %), *n* = 114							$p < 0.001^{\S}$
Strongly disagree	67	(58.8%)	14	(31.8%)	53	(75.7%)	
Disagree	30	(26.3%)	18	(40.9%)	12	(17.1%)	
Neither agree nor disagree	11	(9.6%)	7	(15.9%)	4	(5.7%)	
Agree	5	(4.4%)	4	(9.1%)	1	(1.4%)	
Strongly agree	1	(0.9%)	1	(2.3%)	0	(0.0%)	
Reimbursement of costs: "I think that PrEP should be paid for by the statutory health insurance" (*n*, %), *n* = 114							$p < 0.001^{\S}$
Strongly disagree	8	(7.0%)	5	(11.4%)	3	(4.3%)	
Disagree	9	(7.9%)	6	(13.6%)	3	(4.3%)	
Neither agree nor disagree	16	(14.0%)	13	(29.5%)	3	(4.3%)	
Agree	22	(19.3%)	9	(20.5%)	13	(18.6%)	
Strongly agree	59	(51.8%)	11	(25.0%)	48	(68.6%)	
Attitudes score (0–20) (*n* = 114)							$p < 0.001^{\dagger}$
Mdn (*IQR*)	17.50	(5.00)	14.00	(6.75)	18.00	(4.00)	
M (*SD*)	15.96	(4.01)	13.57	(4.16)	17.46	(3.10)	
Min; *Max*	4-20		4-20		7-20		

IQR, inter quartile range; M, mean; Max, maximum; Mdn, median; Min, minimum; SD, standard deviation. †*From Mann-Whitney U tests of the null hypothesis that the median value of participants from local health offices is equal to that of participants from NG counseling centers.* §*From Pearson's Chi squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, by type of counseling center.*

at-risk clients. This implies that the differences between the two types of centers are mainly explained by different knowledge and counseling skills and attitudes toward PrEP on the side of the individual counselors working in the respective centers. This finding points at the importance of training for the counselors and of supplying material that facilitates counseling on PrEP.

Overall, the counselors participating in the survey indicated that they proactively provided PrEP advice in a mean of 52.0% of sessions with at-risk clients, and it must therefore be assumed that the implementation of the current German and Austrian PrEP guideline has been incomplete so far. This assumption is supported by the fact that, despite of their existence, almost three quarters of the participants indicated that a guideline with a clear presentation of indications, contraindications and necessary laboratory investigations would help to improve PrEP consultations. The wording of the indication for recommending PrEP to MSM and trans persons ("MSM or trans persons who report having had anal sex without condom within the past 3-6 months and/or probably having anal sex without condom in the next months, or who had an STI in the last 12 months,

TABLE 7 | Multiple linear regression to predict the proportion of PrEP advice provided proactively to MSM and trans persons who meet the criteria be offered PrEP according to the German and Austrian guideline (at-risk clients).

Predictors	Coefficient (Robust SE)		Beta	*p*	VIF
Constant	−8.208	(11.468)		0.476	
Knowledge score[1]	1.692	(0.842)	0.221	0.047	1.26
Attitudes score[2]	2.111	(0.910)	0.250	0.022	1.26

SE, standard error; VIF, variance inflation factor. [1]Scale from 0 to 20 points, with higher scores indicating a more positive self-assessment of knowledge about PrEP and counseling competence. [2]Scale from 0 to 20 points, with higher scores indicating a more positive attitudes toward PrEP.

TABLE 8 | Relevance of barriers to PrEP use.

	n	M (SD)		Min-Max
Worries about getting infected with other STIs	111	5.56	(2.73)	0-10
The monthly costs for the PrEP medication	109	5.33	(2.61)	0-10
Lack of information about PrEP in the native language of the client	110	5.10	(3.33)	0-10
The costs for the laboratory investigations	109	4.80	(3.00)	0-10
Worries about mild or temporary side effects	109	4.64	(2.43)	0-10
Time required for regular visits to the doctor	111	4.26	(2.81)	0-10
Worries about severe or permanent side effects	111	4.21	(2.59)	0-10
Lack of information about PrEP in client-friendly language	110	4.17	(2.88)	0-10
Difficulties finding a doctor who prescribes PrEP	112	4.13	(3.64)	0-10
Assessment of the own risk of getting infected with HIV as too low to take PrEP	110	4.08	(2.70)	0-10
Worries about stigmatization in the peer group	107	3.33	(2.67)	0-10
Cultural barriers	110	2.79	(2.51)	0-10

M, mean; Max, maximum; Min, minimum; SD, standard deviation.

respectively," English translation by the authors of the present paper) in the German and Austrian guideline (19) is ambiguous due to the use of unclear operators ("and/or," "respectively") and imprecisely defined time periods ("3-6 months", "next months"). This may be a factor that limits the implementation of the guideline recommendations. The survey revealed that fewer than half of the centers had in-house guidelines or standard operating procedures for PrEP counseling. No information was collected on the content of these in-house guidelines, and it remains unclear whether they contain indications for PrEP advice that deviate from the German and Austrian guidelines. For the purpose of this study, the recommendations of the German and Austrian guideline on HIV pre-exposure prophylaxis were used to define at-risk clients. Whereas one indication to offer PrEP to MSM and trans persons according to the German and Austrian Guideline is a history of an STI in the past 12 months (19), the CDC guidelines on PrEP, for instance, restrict this aspect to the past six months and exclusively to bacterial STIs (18). A narrower definition of the indication to recommend PrEP to MSM and trans people might have led to a higher proportion of proactive PrEP advice in counseling sessions with these clients. It must also be taken into account that the German and Austrian guideline on PrEP has only been available since June 2018, and thus for approximately four months before the data collection for this survey began. This relatively short period of time is probably the most important reason for the incomplete implementation of the guideline recommendations in current counseling practice and for the limited awareness of the guideline found in this survey.

Nonetheless, the incomplete implementation of the current guideline recommendations and the limited awareness of their existence indicate that there is a need and potential for improving and harmonizing counseling on PrEP in counseling centers, particularly when targeting at-risk populations. Bearing this in mind, it is interesting that the counselors who took part in the survey selected mainly client-directed tools as resources that would help to improve PrEP counseling. Among the most frequently selected tools were (1) decision aids for clients that provide information about PrEP in client-friendly or (2) in the client's first language, and (3) an app- or SMS-based reminder system for PrEP users to promote their adherence. In contrast, information or training for counselors was less frequently selected as being helpful for their counseling practice. In line with these results, fewer than half of the participants indicated that they would like to receive training or courses on PrEP counseling. This must be taken into account when deciding on measures to improve targeted counseling on PrEP among counselors in sexual health services.

The focus on client-directed information material and tools when selecting resources that would improve counseling on PrEP reflects that lack of information on the side of potential PrEP users is perceived as one of the most important barriers to initiating PrEP. This barrier can be addressed through the availability of easily understandable information material for clients and especially populations at risk of acquiring HIV. Concerns about sexually transmitted infections, the cost of PrEP medication and follow-up examinations, the lack of information about PrEP in the clients' first languages and worries about mild or temporary side effects were among the barriers for potential PrEP users rated as particularly relevant by the counselors who participated in this survey. This corresponds well with the barriers to taking PrEP found in the Berlin survey among MSM (28). However, aspects such as the costs of PrEP medication and corresponding accompanying examinations as barriers to initiating PrEP are structural barriers. With a law passed in July 2019, the cost of PrEP and necessary laboratory investigations has been covered by public health insurance in Germany since September 2019, which renders this barrier obsolete. Stigmatization of PrEP users by their peers or in their social environments was rated by the counselors as the least relevant barrier, although the aspect of stigmatization was repeatedly mentioned in the free text fields and also in the international literature (38).

Limitations

These insights into PrEP-related knowledge, counseling skills, attitudes, and counseling practice among counselors working in HIV testing and counseling centers can be used to identify and develop strategies for improving PrEP implementation in at-risk

populations. However, there is a number of important limitations to consider when interpreting the results:

Firstly, the questionnaire used in this study was not formally validated before it was used as a survey instrument. PrEP-related knowledge and counseling skills were self-assessed by the participants. We did not present a score that assessed specifically defined levels of competence or skills. It is therefore unclear whether the respective score validly represents the actual knowledge and counseling skills. A systematic review showed that there may be relevant discrepancies between self-assessed knowledge and actual knowledge (39). In addition, no empirical data are available on the question of whether the actual quality of counseling on PrEP is determined primarily by the knowledge of the counselors. However, the fact that there was a significant association between the knowledge score and the attitudes score on one hand, and the proportion of proactive PrEP advice in sessions with at-risk clients on the other, indicate that the knowledge and attitudes scores may be a valid representation of the respective concepts. This is also supported by the good internal consistency of the scores.

Secondly, for pragmatic reasons, the risk groups of "MSM" and "trans persons" were grouped together in the survey. As a result, information may have been lost or recorded inaccurately. The assessment of the counseling practice could lead to different findings if the questions had specifically related to the respective populations separately. Especially with regard to the efficacy and safety of PrEP, far more data are available for MSM than for trans persons (9–12, 14–17, 39). At the same time, for trans persons, other access barriers to health care may be relevant than for MSM—for example, for trans persons, finding a competent physician was described as a particularly relevant barrier to accessing PrEP (40). Furthermore, the sexual orientation of the counselors was not assessed in the survey, although this may have a relevant impact on the PrEP counseling practice and explain differences in this regard between counseling centers and health authorities as an additional variable. We also did not include the primary professional qualification of the counselors in our multiple regression model, as this was not one of the variables that we had chosen a priori, which were limited in number to avoid overfitting.

A third limitation, which pertains to the validity of our findings may be the presence of selection bias. Counselors with little knowledge of or negative attitudes toward PrEP may have been less likely to participate in the survey than counselors with more positive attitudes and/or better knowledge. The extent of such a bias cannot be quantified. In this context, it is worth pointing out that the response rates of 42 and 57% for NG counseling centers and local health offices, respectively, were comparatively high for a survey of this nature. For example, surveys on PrEP among physicians in the USA and the Netherlands had response rates of 23.5 and 39%, respectively (30, 32). While high response rates cannot guarantee unbiased estimates, they do provide less opportunity for selection bias to occur. However, the sample size of the present study is relatively small, also limiting the generalisability of our findings. A further limitation of the representativeness is that only few counseling centers from the new German states (former East Germany) took part in the survey. It must be taken into account that access to HIV tests and advice in rural regions and particularly in the new German states is often only supplied by the local health authorities and only in a small number of NG counseling centers. In contrast, large cities such as Berlin and Hamburg have a higher number of NG counseling centers (34). The regional distribution of the participants in the survey therefore reflects the current situation with respect to sexual health services.

Conclusions

The results of this first survey assessing PrEP-related knowledge, attitudes, and counseling practice among counselors from HIV and STI testing and counseling centers in Germany should be interpreted as baseline data shortly after publication of the German and Austrian guidelines on PrEP. The survey revealed that PrEP counseling in these centers is currently heterogeneous and that the knowledge of and attitudes toward PrEP vary substantially among counselors. In particular, substantial differences were found between counselors from NG counseling centers and the local health offices. Due to the rapid developments in the field of PrEP services in Germany, re-evaluating counseling practice after the guideline recommendations have been available for a longer period and some time after the inclusion of PrEP in the benefits catalog of the public health insurance will probably yield useful findings. In the meantime, concepts that increase the awareness of the guideline recommendations among counselors in the HIV and STI counseling and testing centers in Germany should be developed and implemented. For the comprehensive and successful implementation of HIV prevention strategies with the goal of empowering at-risk populations to take informed decisions, targeted and proactive PrEP advice is a key element. In this regard, there is room for improvement, and both NG counseling centers and the public health authorities should undertake measures to optimize their counselors' knowledge and counseling skills. Bearing in mind that the desire for further training on PrEP counseling was expressed by fewer than half of the counselors who took part in the survey, these measures may focus on decreasing the barriers identified for potential PrEP users, for example by developing and testing resources and tools such as decision-aids for potential PrEP users in client-friendly language and in different languages. Both potential PrEP users and counselors should be included in this process in order to ensure good acceptance and implementation of the tools that are developed.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article/**Supplementary Material**.

ETHICS STATEMENT

The study protocol was reviewed and approved by Ethikkommission der Charité-Universitätsmedizin Berlin.

The participants provided their informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

FK developed the study design and drafted the questionnaire, which was discussed and finalized by FK, RW, MG, MS, and AN. FK led the data collection. FK, MG, and RW conducted the statistical analyses and supported interpretation of results. FK wrote the first draft of the manuscript. All authors provided considerable editing, revisions and content review of the initial manuscript draft, and approved the final draft of the manuscript.

ACKNOWLEDGMENTS

The authors would like to acknowledge and thank all the counselors who participated in the online-survey, as well as the HIV and STI testing and counseling centers (non-governmental counseling centers and local health authorities) who decided to participate in this study. We acknowledge support from the German Research Foundation (DFG) and the Open Access Publication Fund of Charité-Universitätsmedizin Berlin.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2020.00298/full#supplementary-material

Data Sheet S1 | Survey questionnaire (English translation, please note that the questionnaire was only available in German language and the present translation has been undertaken for the publication only).

Data Sheet S2 | Survey questionnaire (original German version).

Table S1 | Minimal underlying data set (Please note that gender, age and years of professional experience of the respondents as well as federal state of the counseling center and qualitative data have been removed to ensure the anonymity of the respondents).

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publication 3: **Sammons MK**, Gaskins M, Kutscha F, Nast A, Werner RN. HIV Pre-exposure Prophylaxis (PrEP): Knowledge, attitudes and counseling practices among physicians in Germany – A cross-sectional survey. PLOS ONE. 2021;16(4):e0250895. doi: 10.1371/journal.pone.0250895.

I conceptualized the study and drafted the questionnaire. I was responsible for the submission of the questionnaires, data collection and entry, the statistical analysis, and wrote the original draft of the publication manuscript.

Journal Data Filtered By: **Selected JCR Year: 2020** Selected Editions: SCIE,SSCI Selected Categories: **"MULTIDISCIPLINARY SCIENCES"** Selected Category Scheme: WoS

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Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	NATURE	915,925	49.962	1.089400
2	SCIENCE	814,971	47.728	0.895760
3	National Science Review	5,889	17.275	0.011400
4	Nature Communications	453,215	14.919	1.238540
5	Science Advances	65,205	14.136	0.218640
6	Nature Human Behaviour	5,549	13.663	0.023120
7	Science Bulletin	8,832	11.780	0.016400
8	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	799,058	11.205	0.806620
9	Journal of Advanced Research	5,927	10.479	0.006800
10	GigaScience	5,876	6.524	0.018630
11	Scientific Data	10,617	6.444	0.034470
12	Frontiers in Bioengineering and Biotechnology	7,470	5.890	0.011340
13	ANNALS OF THE NEW YORK ACADEMY OF SCIENCES	52,619	5.691	0.021430
14	iScience	5,235	5.458	0.012300
15	Research Synthesis Methods	3,926	5.273	0.007520
16	NPJ Microgravity	594	4.415	0.001790
17	Scientific Reports	541,615	4.379	1.232500
18	PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY A-MATHEMATICAL PHYSICAL AND ENGINEERING SCIENCES	24,950	4.226	0.025400

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
19	Journal of the Royal Society Interface	16,834	4.118	0.022010
20	JOURNAL OF KING SAUD UNIVERSITY SCIENCE	3,276	4.011	0.002870
21	Advanced Theory and Simulations	1,201	4.004	0.002780
22	GLOBAL CHALLENGES	1,047	3.847	0.002860
23	FRACTALS-COMPLEX GEOMETRY PATTERNS AND SCALING IN NATURE AND SOCIETY	2,667	3.665	0.002570
24	SCIENCE AND ENGINEERING ETHICS	2,796	3.525	0.003700
25	PROCEEDINGS OF THE JAPAN ACADEMY SERIES B-PHYSICAL AND BIOLOGICAL SCIENCES	2,218	3.493	0.001940
26	PLoS One	357,723	3.240	1.081150
27	PeerJ	29,906	2.984	0.069540
28	Royal Society Open Science	11,155	2.963	0.030990
29	INTERNATIONAL JOURNAL OF BIFURCATION AND CHAOS	8,572	2.836	0.006590
30	COMPLEXITY	7,133	2.833	0.009620
31	SCIENCE PROGRESS	689	2.774	0.000380
32	JOURNAL OF THE ROYAL SOCIETY OF NEW ZEALAND	944	2.750	0.000680
33	Symmetry-Basel	9,999	2.713	0.011650
34	PROCEEDINGS OF THE ROYAL SOCIETY A-MATHEMATICAL PHYSICAL AND ENGINEERING SCIENCES	22,295	2.704	0.015330
35	Journal of Taibah University for Science	2,141	2.688	0.002210
36	MIT Technology Review	1,156	2.563	0.002680
37	Facets	488	2.535	0.001170

Selected JCR Year: 2020; Selected Categories: "MULTIDISCIPLINARY SCIENCES"

PLOS ONE

RESEARCH ARTICLE

HIV Pre-exposure Prophylaxis (PrEP): Knowledge, attitudes and counseling practices among physicians in Germany – A cross-sectional survey

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OPEN ACCESS

Citation: Sammons MK, Gaskins M, Kutscha F, Nast A, Werner RN (2021) HIV Pre-exposure Prophylaxis (PrEP): Knowledge, attitudes and counseling practices among physicians in Germany – A cross-sectional survey. PLoS ONE 16(4): e0250895. https://doi.org/10.1371/journal.pone.0250895

Editor: Kingston Rajiah, International Medical University, MALAYSIA

Received: January 25, 2021

Accepted: April 15, 2021

Published: April 29, 2021

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0250895

Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files: We uploaded the minimal

Abstract

Background

German statutory health insurance began covering the costs associated with HIV PrEP in September 2019; however, to bill for PrEP services, physicians in Germany must either be certified as HIV-specialists according to a nationwide quality assurance agreement, or, if they are non-HIV-specialists, have completed substantial further training in HIV/PrEP care. Given the insufficient implementation of PrEP, the aim of our study was to explore the potential to increase the number of non-HIV-specialists providing PrEP-related services.

Methods

We conducted an anonymous survey among a random sample of internists, general practitioners, dermatologists and urologists throughout Germany using a self-developed questionnaire. We calculated a knowledge score and an attitudes score from individual items in these two domains. Both scores ranged from 0–20, with high values representing good knowledge or positive attitudes. We also asked participants about the proportion of PrEP advice they provided proactively to men who have sex with men (MSM) and trans-persons who met the criteria to be offered PrEP.

Results

154 physicians completed the questionnaire. Self-assessed knowledge among HIV-specialists was greater than among non-HIV-specialists [*Median* knowledge score: 20.0 (*IQR* = 0.0) vs. 4.0 (*IQR* = 11.0), $p<0.001$]. Likewise, attitudes towards PrEP were more positive among HIV-specialists than non-HIV-specialists [*Median* attitudes score: 18.0 (*IQR* = 3.0) vs. 13.0 (*IQR* = 5.25), $p<0.001$]. The proportion of proactive advice on PrEP provided to at-risk MSM and trans-persons by HIV-specialists [*Median*: 30.0% (*IQR* = 63.5%)] was higher than that provided by non-HIV-specialists [*Median*: 0.0% (*IQR* = 11.3%), $p<0.001$].

underlying data set and codebook (Supporting file S3). Age of respondents, postal code, state and qualitative data have been removed to ensure anonymity.

Funding: The authors received no specific funding for this work. We acknowledge support from the Open Access Publication Fund of Charité – Universitätsmedizin Berlin.

Competing interests: The authors have declared that no competing interests exist.

However, the results of our multiple regression suggest the only independent predictor of proactive PrEP advice was the knowledge score, and not whether physicians were HIV-specialists or non-HIV-specialists.

Conclusions

These findings point to opportunities to improve PrEP implementation in individuals at risk of acquiring HIV. Targeted training, particularly for non-HIV-specialists, and the provision of patient-centered information material could help improve care, especially in rural areas.

Introduction

HIV pre-exposure prophylaxis (PrEP) consisting of tenofovir disoproxil fumarate and emtricitabine has been approved for HIV prevention in the United States since 2012 and in the European Union since 2016. Its high effectiveness and safety have been demonstrated in several randomized controlled trials [1–4], and observational studies in a number of metropolitan regions have shown dramatic reductions in the incidence of HIV infections, especially in men who have sex with men (MSM), in recent years–a substantial proportion of which is likely due to PrEP [5–10].

Despite these developments, the uptake of PrEP among those at high risk of HIV acquisition has been slow. By 2019 approximately 224,000 people in the US were estimated to have received a prescription for PrEP, representing only a small fraction of the 1.1 million individuals calculated by researchers at the US Centers for Disease Control and Prevention (CDC) to have an indication for it [11–13]. In Europe, a 2019 study based on data from the European MSM Internet Survey found that an estimated 17.4% of MSM, or 500,000 individuals, in the EU who were very likely to use PrEP were not able to access it [14]. Improving the uptake of PrEP therefore remains a key public health priority.

The German system of statutory health insurance began covering the costs associated with HIV pre-exposure prophylaxis (PrEP) in September 2019. In order to be able to bill for PrEP-related appointments and testing costs, however, physicians in Germany must either be certified according to the German Quality Assurance Agreement on HIV/AIDS as HIV specialists or, if they are non-HIV specialists and belong to certain specialties (e.g., internal and general medicine, dermatology and urology), have completed further training on HIV and PrEP [15]. The training consists of taking part in a 16-hour internship in an outpatient or inpatient HIV care facility and being present during consultations with at least 15 persons who are either living with HIV/AIDS or considering or taking PrEP. In addition, proof of participation in further training courses on the topic must be provided [15]. Because many physicians in Germany work in regions that do not have an outpatient or inpatient HIV treatment facility, the certification requirements represent a substantial barrier to providing PrEP care. This could potentially lead to gaps in treatment, particularly in smaller towns and rural areas, where HIV specialist centers are rare [16].

Given the insufficient implementation of PrEP in populations at risk of acquiring HIV in Germany [17, 18] and beyond, the aim of our study was to explore the potential to increase the number of non-HIV-specialists prescribing PrEP by reducing the barriers to their completing further training. We therefore sought to examine and compare, among HIV-specialists and non-HIV-specialists, self-assessed knowledge and attitudes towards PrEP, as well as the proportion of PrEP advice provided proactively to men who have sex with men (MSM) and trans

persons who met the criteria to be offered PrEP according to the German and Austrian PrEP guideline ("at-risk patients"). Such information could be useful for identifying opportunities to improve PrEP implementation in individuals at risk of acquiring HIV, particularly those in regions underserved by HIV-specialists.

Materials and methods

Study design

We conducted a survey among office-based general practitioners, internists, infectious disease specialists, dermato-venereologists and urologists in Germany. Data was collected from August to October 2019. The study was approved by the institutional ethics board of Charité —Universitätsmedizin Berlin (EA1/006/19). Participation was voluntary and no incentives were provided. All participants were older than 18 years. Participants in the online survey provided their written informed consent by ticking the box next to a statement that they had read the study information and agreed to participate in the study. For participants who completed the paper version of the survey, we assumed consent if they returned their questionnaire by fax or mail.

Setting and participants

Physicians in the abovementioned groups in Germany were eligible to participate in the survey. We classified participants as HIV-specialists if they indicated that they worked in an HIV-specialty practice, and as non-HIV-specialists if they indicated that they did not to work in such a practice. HIV specialist practices in Berlin are owned and staffed primarily by doctors certified as HIV-specialists according to the German Quality Assurance Agreement on HIV/AIDS, and visiting these practices usually requires an appointment. They provide a range of generalist and sexual health care to LGBTI+ people whether or not these individuals are living with HIV.

We used various strategies to recruit participants: (1) We requested the contact details of a random sample of 2,200 office-based physicians in the eligible specialties from the National Association of Statutory Health Insurance Physicians (Kassenärztliche Bundesvereinigung, KBV). We mailed these physicians a paper version of our questionnaire, which could be returned to us by fax or mail. A reminder email with a link to an online version of the questionnaire was sent to the 926 (42%) physicians in this sample for whom we had an email address; (2) An invitation to participate in the survey, containing a link to the online version of the questionnaire, was sent to 253 members of the German AIDS Society (Deutsche AIDS Gesellschaft, DAIG) and to 330 members of the German STI Society (Deutsche STI Gesellschaft, DSTIG) via their online mailing lists. A reminder email was sent two weeks after the initial invitation; (3) Additionally, we placed flyers advertising our study at a Berlin STI conference in September 2019. All online surveys were completely anonymous, with neither IP addresses nor email addresses recorded.

Variables and measurements

A standardized German-language questionnaire exploring PrEP knowledge, attitudes and counselling practices among physicians in Germany was not available. We therefore developed the questionnaire for the purposes of the present study (S1 and S2 Files). The original draft questionnaire (MS) was tested and discussed (RW, MG, FK) to identify and solve any problems concerning the comprehensibility of the content and design, and to ensure alignment with a related questionnaire we developed to explore PrEP knowledge, attitudes and counselling practices among non-governmental counselling centres and local health offices in Germany. The results of this latter study are published elsewhere [19].

Demographic data included medical specialty, whether the practice had been certified according to the Quality Assurance Agreement on HIV/AIDS, age, gender and languages spoken. The first three numbers of the practice zip codes were recorded to determine in which of Germany's 16 states the practice was located. To obtain contextual information about the practice, we asked how many (a) HIV tests had been performed, (b) HIV infections diagnosed and (c) MSM and transgender patients seen within an average calendar quarter (3 months).

After providing a brief summary of the recommendations of the German and Austrian guideline [20] on the indications for offering PrEP to HIV-negative MSM and transgender persons (which served as our definition of "at-risk patients"), we asked participants to indicate the number of patients they saw during an average quarter who fulfilled these criteria and the number of these patients who were provided with advice on PrEP proactively by the physician. Self-assessed knowledge about PrEP and self-reported attitudes towards PrEP were quantified as described in our previous study [19]. This comprised the calculation of a summative knowledge score and a summative attitudes score from five individual knowledge and attitude items, respectively. The total scores ranged from 0 and 20, with high values representing good knowledge or positive attitudes toward PrEP, respectively. Furthermore, we presented a list of various aspects that might be perceived as barriers to patients initiating PrEP and asked participants to rate the relevance of each of these aspects on an 11-level rating scale. This included barriers for the patients as assessed in the previous study [19], as well as additional barriers for physicians. Lastly, we asked participants which training or information materials would help them with PrEP advice and prescriptions [19].

Sample size and statistical methods

The questionnaire was developed for the purposes of this study, and no data were available on expected means or variability. Therefore, no sample size calculation was performed and the size of the random sample (n = 2,200) was based on feasibility considerations. Statistical analyses were performed using IBM® SPSS® Statistics version 25 (sample characteristics and bivariate statistics) and STATA SE version 14.2 (linear regression). Independent t-tests, Mann-Whitney U-tests, Pearson's chi squared tests and Fisher's Exact tests were used to quantify associations between variables, depending on the distribution and type of data.

We performed a multiple linear regression using both backward and forward elimination to identify predictors of the proportion of proactive advice on PrEP that had been provided during appointments with at-risk patients. The following variables for the regression model were purposefully selected a priori: HIV specialist status (HIV-specialists vs. non-HIV-specialists), size of the city in which the physician's practice was located, location in either a western or eastern German state (with eastern states being defined as any of the five new states formed from the territory of former East Germany as part of German reunification in 1990), gender, percentage of positive HIV tests (number of positive tests/total number of patients tested), knowledge score and attitudes score. The stopping rule for eliminating individual variables in the logistic regression was $p<0.2$. Variance inflation factor (VIF) statistics, tolerance and condition index were used to ensure that there was no multi-collinearity of the predictors or instability of the regression coefficients. Missing cases were excluded in a listwise fashion. The level for statistical significance was set at $p<0.05$.

Results

Demographic data

We received a total of 161 responses, of which we excluded seven because they did not provide meaningful information. The sample included in our analyses therefore consisted of 154

respondents, 72 of whom indicated that they worked in an HIV-specialty practice and 79 of whom indicated that they did not work in such a practice ("non-HIV-specialists"). Three participants did not provide information about their HIV specialist status or medical specialty; data from these participants were included only in the analyses of barriers to the prescription of PrEP and of helpful materials and training. Demographic data of the sample, including tests for differences according to HIV specialist status, are shown in *Table 1*. Statistically significant associations between HIV specialist status and demographic data were found for gender ($\chi^2(df = 1, n = 151) = 6.938$, $p = 0.008$), specialty ($\chi^2(df = 5, n = 151) = 83.379$, $p<0.001$), size of the city in which the practice was located ($\chi^2(df = 3, n = 142) = 33.378$, $p<0.001$), and the state in which the practice was located (i.e., eastern states vs. western states) ($\chi^2(df = 1, n = 142) = 3.833$, $p = 0.05$).

Physician appointments with at-risk patients and HIV testing practice

Table 2 depicts data on the number of (a) appointments with MSM and trans persons overall, (b) appointments with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guideline ("at-risk patients"), (c) the overall number of HIV tests and (d) the number and proportion of positive HIV tests per quarter as indicated by the respondents. For all of the mentioned variables, we found statistically significant differences between HIV-specialists and non-HIV-specialists.

Independent of their HIV specialist status, the respondents indicated that in a median of 15.5% of their appointments with at-risk patients, they proactively provided advice on PrEP (*Table 3*). The proportion of appointments with at-risk patients in which the physician provided proactive advice on PrEP was significantly higher among HIV-specialists than it was among non-HIV-specialists: HIV-specialists indicated that they proactively provided advice on PrEP in a median of 30.0% of their contacts with at-risk patients, whereas non-HIV-specialists indicated that they proactively provided advice on PrEP in a median of 0.0% of their contacts, $U = 468.500$, $p<0.001$.

Self-assessment of PrEP knowledge and advising competence

For each of the self-assessed dimensions of knowledge and competence, the participants in our survey tended to agree with the relevant statements in the questionnaire if they were HIV-specialists, whereas they tended to disagree with these statements if they were non-HIV-specialists. These differences were found to be statistically significant (*Table 4*). Correspondingly, the summative knowledge score was higher for HIV-specialists (*Median* = 20.0, *IQR* = 0.0) than it was for non-HIV-specialists (*Median* = 4.0, *IQR* = 11.0), $U = 279.0$, $p<0.001$.

Attitudes towards PrEP

Regarding attitudes towards PrEP, we found that HIV-specialists agreed with all of the statements expressing a positive attitude and disagreed with the statement expressing a negative attitude more often than the non-HIV-specialists (*Table 5*). As with the summative knowledge score reported above, the summative attitudes score was higher among HIV-specialists (*Median* = 18.0, *IQR* = 3.0) than among non-HIV-specialists (*Median* = 13.0, *IQR* = 5.25), $U = 588$, $p<0.001$.

Multiple linear regression on the proportion of proactive PrEP advice

To determine independent factors that predicted the proportion of PrEP advice provided proactively by physicians to at-risk patients, we developed a multiple linear regression model. Applying both a backward elimination and a stepwise forward elimination method (both with a stopping rule of $p<0.2$ for the exclusion or inclusion of each variable), the same regression

Table 1. Demographic data and contextual characteristics of the sample.

Variable		Total sample		HIV specialist status			
				HIV-specialists		Non-HIV-specialists	
N		154*		72		79	
Age in years (n = 145)							$p = 0.180^{\dagger}$
	Mean (*SD*)	52.22	(8.98)	51.20	(8.46)	53.20	(9.39)
	Min; *Max*	33–84		34–76		33–84	
Gender (***n***, %)							$p = 0.008^{\$}$
	Female	54	(35.1%)	18	(25.0%)	36	(45.6%)
	Male	97	(63.0%)	54	(75.0%)	43	(54.4%)
	Not specified	3	(1.9%)	0	(0.0%)	0	(0.0%)
Specialty (***n***, %)							$p < 0.001^{\$}$
	General Medicine	35	(22.7%)	11	(15.3%)	24	(30.4%)
	Internal Medicine	27	(17.5%)	22	(30.6%)	5	(6.3%)
	Dermatology	25	(16.2%)	4	(5.6%)	21	(26.6%)
	Urology	25	(16.2%)	0	(0.0%)	25	(31.6%)
	General Medicine and Internal Medicine with Additional Qualification for Infectious Disease	37	(24.0%)	35	(48.6%)	2	(2.5%)
	Not specified	5	(3.4%)	0	(0.0%)	2	(2.5%)
Size of city (***n***, %)							$p < 0.001^{\$}$
	Metropolis (>1,000,000)	52	(33.8%)	36	(50.0%)	16	(20.3%)
	Large city (>100,000)	44	(28.6%)	25	(34.7%)	19	(24.1%)
	City (>10,000)	27	(17.5%)	4	(5.6%)	23	(29.1%)
	Small city (≤ 10,000)	19	(12.3%)	2	(2.8%)	17	(21.5%)
	Not specified	12	(7.8%)	5	(6.9%)	4	(5.1%)
State (***n***, %)							$p = 0.05^{\#}$
	Western German states, including Berlin	**123**	**(79.9%)**	**62**	**(86.1%)**	**61**	**(77.2%)**
	Baden-Wuerttemberg	15	(9.7%)	8	(11.1%)	7	(8.9%)
	Bavaria	18	(11.7%)	13	(18.1%)	5	(6.3%)
	Berlin	26	(16.9%)	14	(19.4%)	12	(15.2%)
	Bremen	2	(1.3%)	0	(0%)	2	(2.5%)
	Hamburg	5	(3.2%)	4	(5.6%)	1	(1.3%)
	Hesse	23	(14.9%)	12	(16.7%)	11	(13.9%)
	Lower Saxony	5	(3.2%)	0	(0.0%)	5	(6.3%)
	North Rhine-Westphalia	22	(14.3%)	10	(13.9%)	12	(15.2%)
	Rhineland-Palatinate	5	(3.2%)	1	(1.4%)	4	(5.1%)
	Saarland	2	(1.3%)	0	(0.0%)	2	(2.5%)
	Schleswig-Holstein	0	(0.0%)	0	(0.0%)	0	(0.0%)
	Eastern German states, excluding Berlin	**19**	**(12.3%)**	**5**	**(6.9%)**	**14**	**(17.7%)**
	Brandenburg	2	(1.3%)	0	(0.0%)	2	(2.5%)
	Mecklenburg-Western Pomerania	1	(0.6%)	0	(0.0%)	1	(1.3%)
	Saxony	7	(4.5%)	3	(4.2%)	4	(5.1%)
	Saxony-Anhalt	5	(3.2%)	0	(0.0%)	5	(6.3%)
	Thuringia	4	(2.6%)	2	(2.8%)	2	(2.5%)
	Not specified	12	(7.8%)	5	(6.9%)	4	(5.1%)

Max, maximum; *Min*, minimum; *SD*, standard deviation;

*3 patients who were included in some of the analyses in the present study did not provide information about their specialist status (HIV-specialists vs. non-HIV-specialists);

†From independent samples t-tests of the null hypothesis that the mean value of non-HIV-specialists is equal to that of HIV specialists;

$From Pearson's Chi squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, according to the HIV specialist status;

#From Pearson's Chi squared tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in the categories "western German states" vs. "eastern German states", according to the HIV specialist status.

https://doi.org/10.1371/journal.pone.0250895.t001

Table 2. Number of appointments with different categories of patients and HIV-tests per calendar quarter.

				HIV specialist status			
Variable		**Total sample**		**HIV-specialists**		**Non-HIV-specialists**	
Number of overall appointments with MSM and trans persons per quarter (n = 141)							$p < 0.001^{\dagger}$
	Median (IQR)	30.0	(345.0)	375.0	(400.0)	5.0	(18.0)
	Mean (*SD*)	162.50	(213.05)	327.88	(210.47)	16.97	(33.20)
	Q1 –*Q3*	5.0–350.0		100.0–500.0		2.0–20.0	
Number of appointments with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guideline (at-risk clients) per quarter (n = 131)							$p < 0.001^{\dagger}$
	Median (IQR)	17.0	(99.0)	100.0	(170.0)	1.0	(6.0)
	Mean (*SD*)	71.74	(114.08)	143.60	(132.33)	7.17	(15.33)
	Q1 –*Q3*	1.0–100.0		30.0–200.0		0.0–6.0	
Overall number of HIV tests per quarter (n = 145)							$p < 0.001^{\dagger}$
	Median (IQR)	20.0	(87.0)	80.0	(195.0)	4.0	(17.7)
	Mean (*SD*)	73.14	(124.03)	139.94	(152.79)	12.50	(23.21)
	Q1 –*Q3*	3.0–90.0		30.0–225.0		1.0–18.7	
Number of positive HIV test results per quarter (n = 143)							$p < 0.001^{\dagger}$
	Median (IQR)	1.0	(2.0)	2.0	(4.0)	0.0	(1.0)
	Mean (*SD*)	5.64	(30.46)	11.45	(43.93)	0.51	(1.36)
	Q1 –*Q3*	0.0–2.0		1.0–5.0		0.0–1.0	
Proportion of positive HIV test results among overall number of HIV tests per quarter (n = 140)							$p < 0.001^{\dagger}$
	Median (IQR)	1.63%	(6.50%)	2.83%	(8.73%)	0.00%	(5.00%)
	Mean (*SD*)	6.47%	(12.41%)	8.02%	(10.16%)	5.16%	(13.96%)
	Q1 –*Q3*	0.00%-6.50%		1.27%-10.00%		0.00%-5.00%	

IQR, interquartile range; *Q1*, first quartile; *Q3*, third quartile;

†From Mann-Whitney U-tests of the null hypothesis that the median value of HIV specialists is equal to that of non HIV specialists.

https://doi.org/10.1371/journal.pone.0250895.t002

equation was found ($F(3,79) = 7.70$, $p<0.001$, $n = 83$), with $R^2 = 0.165$ (*Table 6*). Only the city size, knowledge score and attitudes score remained in the model; ultimately, however, the only statistically significant predictor was the knowledge score.

Educational materials and barriers

In total, 121 participants answered the question about which materials or tools they thought would increase the practicability of their PrEP counselling and prescriptions. Patient decision

Table 3. Advice on PrEP during appointments with MSM and trans persons who met the criteria to be offered PrEP according to the German and Austrian guideline (at-risk patients).

		Total sample		HIV specialist status			
Variable				**HIV-specialists**		**Non-HIV-specialists**	
Proportion of appointments with 'at-risk' MSM and trans persons in which physicians themselves proactively address the topic PrEP (n = 102)							$p < 0.001^{\dagger}$
	Median (IQR)	15.48%	(50.0%)	30.00%	(63.50%)	0.00%	(11.32%)
	Mean (SD)	30.20%	(35.34%)	40.70%	(34.21%)	16.36%	(32.21%)
	Q1 –*Q3*	0.00% - 50.00%		11.50% - 75.00%		0.00% - 11.32%	

IQR, interquartile range; *Q1*, first quartile; *Q3*, third quartile; *SD*, standard deviation;

†From Mann-Whitney U-tests of the null hypothesis that the median value of HIV-specialists is equal to that of non-HIV-specialists.

https://doi.org/10.1371/journal.pone.0250895.t003

Table 4. Self-assessment of knowledge and counselling competence.

Variable		Total sample		HIV specialist status			
				HIV-specialists		Non-HIV-specialists	
Global assessment: "I am well-informed about PrEP" (n, %), $n = 128$							$p < 0.001^{\dagger}$
	Strongly disagree	31	(24.2%)	1	(1.8%)	30	(42.3%)
	Disagree	17	(13.3%)	0	(0.0%)	17	(23.9%)
	Neither agree nor disagree	6	(4.7%)	1	(1.8%)	5	(7.0%)
	Agree	16	(12.5%)	4	(7.0%)	12	(16.9%)
	Strongly agree	58	(45.3%)	51	(89.5%)	7	(9.9%)
Indications: "I am able to comprehensively give patients advice on whether it makes sense to take PrEP in their respective case" (n, %), $n = 128$							$p < 0.001^{\dagger}$
	Strongly disagree	23	(18.0%)	1	(1.8%)	22	(31.0%)
	Disagree	22	(17.2%)	0	(0.0%)	22	(31.0%)
	Neither agree nor disagree	10	(7.8%)	1	(1.8%)	9	(12.7%)
	Agree	15	(11.7%)	5	(8.8%)	10	(14.1%)
	Strongly agree	58	(45.3%)	50	(87.7%)	8	(11.3%)
Adverse effects: "I am able to comprehensively give patients advice on the adverse effects of PrEP" (n, %), $n = 128$							$p < 0.001^{\dagger}$
	Strongly disagree	31	(24.2%)	1	(1.8%)	30	(42.3%)
	Disagree	19	(14.8%)	0	(0.0%)	19	(26.8%)
	Neither agree nor disagree	7	(5.5%)	0	(0.0%)	7	(9.9%)
	Agree	11	(8.6%)	3	(5.3%)	8	(11.3%)
	Strongly agree	60	(46.9%)	53	(93.0%)	7	(9.9%)
Modalities of intake: "I am able to comprehensively give patients advice on the possible modalities of intake of PrEP (e.g., continuous vs. on-demand)" (n, %), $n = 128$							$p < 0.001^{\dagger}$
	Strongly disagree	31	(24.2%)	1	(1.8%)	30	(42.3%)
	Disagree	20	(15.6%)	0	(0.0%)	20	(28.2%)
	Neither agree nor disagree	5	(3.9%)	1	(1.8%)	4	(5.6%)
	Agree	10	(7.8%)	2	(3.5%)	8	(11.3%)
	Strongly agree	62	(48.4%)	53	(93.0%)	9	(12.7%)
Investigations: "I am able to comprehensively give patients advice on the medical investigations necessary during the use of PrEP" (n, %), $n = 128$							$p < 0.001^{\dagger}$
	Strongly disagree	29	(22.7%)	1	(1.8%)	28	(39.4%)
	Disagree	20	(15.6%)	0	(0.0%)	20	(28.2%)
	Neither agree nor disagree	6	(4.7%)	1	(1.8%)	5	(7.0%)
	Agree	9	(7.0%)	2	(3.5%)	7	(9.9%)
	Strongly agree	64	(50.0%)	53	(93.0%)	11	(15.5%)
Knowledge score (0–20), $n = 128$							$p < 0.001^{\#}$
	Median (*IQR*)	15.0	(17.0)	20.0	(0.0)	4.0	(11.0)
	Mean (*SD*)	11.89	(8.43)	19.23	(2.96)	6.49	(6.76)
	Q1 –*Q3*	3.0–20.0		20.0–20.0		0.0–11.0	

Max, maximum; *Min*, minimum; *IQR*, interquartile range; *Q1*, first quartile; *Q3*, third quartile;

[†]From Fisher's Exact tests of the null hypothesis that there is no statistically significant difference between the observed and expected frequencies in each category, by physician group.

[#]From Mann-Whitney U-tests of the null hypothesis that the median value of HIV-specialists is equal to that of non-HIV-specialists.

https://doi.org/10.1371/journal.pone.0250895.t004

aids that present information on PrEP in patient-friendly language (71.9%, $n = 87$) and in different languages (56.2%, $n = 68$) were chosen most frequently. About half of the respondents (53.7%, $n = 65$) indicated that a national guideline containing a clear presentation of indications, contraindications and laboratory investigations would be helpful. Whereas about half of

Table 5. Attitudes towards PrEP.

Variable		Total sample		HIV specialist status			
				HIV-specialists		Non-HIV-specialists	
Global assessment: "I think that PrEP is an important element of HIV prevention strategies" (n, %), *n* = 126							$p < 0.001^{\$}$
	Strongly disagree	1	(0.8%)	0	(0.0%)	1	(1.4%)
	Disagree	7	(5.6%)	1	(1.8%)	6	(8.7%)
	Neither agree nor disagree	10	(7.9%)	1	(1.8%)	9	(13.0%)
	Agree	30	(23.8%)	4	(7.0%)	26	(37.7%)
	Strongly agree	78	(61.9%)	51	(89.5%)	27	(39.1%)
Reliability: "I think that PrEP is a reliable method to protect oneself from HIV" (n, %), *n* = 124							$p < 0.001^{\$}$
	Strongly disagree	5	(4.0%)	0	(0.0%)	5	(7.5%)
	Disagree	8	(6.5%)	0	(0.0%)	8	(11.9%)
	Neither agree nor disagree	19	(15.3%)	4	(7.0%)	15	(22.4%)
	Agree	44	(35.5%)	16	(28.1%)	28	(41.8%)
	Strongly agree	48	(38.7%)	37	(64.9%)	11	(16.4%)
Adverse effects: "I think that PrEP is a method to protect oneself from HIV that has few side effects" (n, %), *n* = 124							$p < 0.001^{\$}$
	Strongly disagree	5	(4.0%)	0	(0.0%)	5	(7.4%)
	Disagree	19	(15.3%)	2	(3.6%)	17	(25.0%)
	Neither agree nor disagree	36	(29.0%)	11	(19.6%)	25	(36.8%)
	Agree	37	(29.8%)	21	(37.5%)	16	(23.5%)
	Strongly agree	27	(21.8%)	22	(39.3%)	5	(7.4%)
Availability of better alternatives: "I think that PrEP is unnecessary, because there are better alternatives to protect oneself from HIV" (n, %), *n* = 121							$p = 0.003^{\$}$
	Strongly disagree	54	(44.6%)	34	(59.6%)	20	(31.3%)
	Disagree	38	(31.4%)	17	(29.8%)	21	(32.8%)
	Neither agree nor disagree	23	(19.0%)	5	(8.8%)	18	(28.1%)
	Agree	3	(2.5%)	1	(1.8%)	2	(3.1%)
	Strongly agree	3	(2.5%)	0	(0.0%)	3	(4.7%)
Reimbursement of costs: "I think that PrEP should be paid for by the statutory health insurance" (n, %), *n* = 124							$p = 0.001^{\$}$
	Strongly disagree	10	(8.1%)	1	(1.8%)	9	(13.4%)
	Disagree	15	(12.1%)	3	(5.3%)	12	(17.9%)
	Neither agree nor disagree	23	(18.5%)	10	(17.5%)	13	(19.4%)
	Agree	25	(20.2%)	9	(15.8%)	16	(23.9%)
	Strongly agree	51	(41.1%)	34	(59.6%)	17	(25.4%)
Attitude Score (0–20), *n* = 118							$p < 0.001^{\dagger}$
	Median (*IQR*)	15.5	(5.0)	18.0	(3.0)	13.0	(5.25)
	Mean (*SD*)	14.93	(3.92)	17.29	(2.59)	12.90	(3.78)
	Q1 –Q3	13.0–18.0		16.0–19.0		10.0–15.25	

IQR, interquartile range; *Q1*, first quartile; *Q3*, third quartile;

[†]From Mann-Whitney U-tests of the null hypothesis that the median value of HIV-specialists is equal to that of non-HIV-specialists

[$]From Fisher's Exact tests of the null hypothesis stating that there is no statistically significant difference between the observed and expected frequencies in each category, according to physician group.

https://doi.org/10.1371/journal.pone.0250895.t005

the respondents (53.7%, *n* = 65) indicated that educational material or training on the management of PrEP would be useful for their practice, fewer indicated that educational material or training on identifying PrEP candidates (38.8%, *n* = 47) or on talking with patients about sex (29.8%, *n* = 36) would be helpful. However, significantly more non-HIV-specialists than HIV-specialists indicated that they wished to receive educational material or training on how to

Table 6. Multiple linear regression to predict the proportion of PrEP advice provided proactively to MSM and trans persons who meet the criteria be offered PrEP according to the German and Austrian guideline (at-risk patients).

Predictors	Coefficient (*Robust SE*)		Beta	*p*	*VIF*
Constant	-32.632	(16.238)		0.048	
Size of the city [1]	6,107	(4.553)	0.170	0.184	1.39
Knowledge score[2]	1,782	(0.585)	0.320	0.003	2.00
Attitudes score[3]	1.851	(1.031)	0.191	0.077	1.57

SE, standard error; *VIF*, variance inflation factor; [1] Size of the city coded in 4 categories with 0 indicating more than 1,000,000 inhabitants and 3 indicating less than 10,000 inhabitants [2] Scale from 0 to 20 points, with higher scores indicating a more positive self-assessment of knowledge about PrEP and counselling competence; [3] Scale from 0 to 20 points, with higher scores indicating a more positive attitude towards PrEP.

https://doi.org/10.1371/journal.pone.0250895.t006

manage PrEP users (61.9% vs. 43.6%, $\chi^2(df = 1, n = 118) = 3.938$, $p = 0.047$) and to identify PrEP candidates (50.8% vs. 25.5%, $\chi^2(df = 1, n = 118) = 7.926$, $p = 0.005$). Less than half of the respondents (45.5%, $n = 55$) indicated that an app- or text-message-based reminder service for patients would be useful to increase the adherence of PrEP users.

When respondents were asked to rate the relevance of barriers for patients to initiate PrEP, they rated the following as the most relevant: patients underestimating their own risk of acquiring HIV infection (*Median* = 8.00, *IQR* = 4.0), difficulties in finding a doctor to prescribe PrEP (*Median* = 8.00, *IQR* = 5.5) and the time required for regular visits to the doctor (*Median* = 7.0, *IQR* = 6.0). Further results on perceived barriers to PrEP initiation and their relevance for patients are shown in ***Table 7***. Among the barriers for physicians, respondents indicated that time-consuming management of PrEP patients was a relevant barrier (*Median* = 7.0, *IQR* = 4.0), but that difficulties identifying those who would benefit from PrEP were less relevant (*Median* = 3.0, *IQR* = 6.0).

Discussion

Our study is the first of its kind to assess physicians' knowledge of HIV PrEP, their attitudes towards it, and their counseling practices in consultations with patients across Germany who are interested in or have indications for PrEP. Given the large gap, in the EU and beyond, between individuals who are interested in using PrEP but are unable to access it, we aimed to explore with our survey whether there might be potential to increase the number of non-HIV-

Table 7. Barriers for patients to initiate PrEP as perceived by participating physicians.

	n	*Median* (*IQR*)	
Assessment of the own risk of getting infected with HIV as too low to take PrEP	69	8.0	(4.0)
Difficulties finding a doctor who prescribes PrEP	74	8.0	(5.5)
Time required for regular visits to the doctor	66	6.0	(6.0)
The monthly costs of the PrEP medication	69	6.0	(6.0)
Lack of information about PrEP in patient-friendly language	68	5.0	(5.0)
Lack of information about PrEP in the native language of the client	68	5.0	(5.0)
Worries about getting infected with other STIs	71	5.0	(5.0)
Cultural barriers	72	5.0	(6.0)
The costs of the laboratory tests	73	5.0	(6.0)
Worries about severe or permanent side effects	68	4.0	(5.0)
Worries about mild or temporary side effects	67	3.0	(4.0)
Worries about stigmatization in the peer group	69	3.0	(5.0)

https://doi.org/10.1371/journal.pone.0250895.t007

specialists providing PrEP-related services in Germany by reducing the barriers to their completing further training and thus being able to bill for these services.

It is therefore highly relevant that participants in our survey rated "difficulties in finding a doctor who prescribes PrEP" as one of the most important barriers for patients to initiate chemoprophylaxis. The lack of HIV-specialists in rural areas is well-reflected in our study, with more than 80% of HIV-specialists who responded to our survey indicating that they were located in cities with more than 100,000 and 50% indicating that they were located in cities with more than 1 million inhabitants. Conversely, more than 50% of the non-HIV-specialists participating in our study reported that they were located in cities with fewer than 100,000 inhabitants. Any opportunity to increase the number of non-HIV-specialists who can give advice on PrEP and prescribe PrEP to patients at risk of acquiring HIV in conformity with the relevant guidelines should therefore be explored. The same can be said of the gap between the western and eastern German states more generally, where a decades-long tradition of large HIV-specialty practices and community-based counselling centers in the west contrasts with a lack of such facilities and institutions in the east.

As expected, our results suggest that HIV-specialists have greater knowledge and counseling competence related to PrEP, as well as more positive attitudes towards it, than do non-HIV-specialists. Unsurprisingly, a greater proportion of patients who had an indication for PrEP were proactively given advice on it by the HIV-specialists. This being said, attitudes towards PrEP and particularly knowledge of it were much more heterogeneous among our participating non-HIV-specialists than was the case among HIV-specialists, which suggests that at least some of the non-HIV-specialists in our sample might require little or no training on PrEP care. Indeed, the results of our multiple linear regression suggest that knowledge of PrEP was the only statistically significant predictor of the proportion of indicated patients who were proactively given advice and counseling on PrEP by participating physicians. It might therefore be wise for policymakers and other actors in the German health system to consider providing non-HIV-specialists who fit this description, particularly if they are in a rural location, with ways to demonstrate and certify their skills that are less onerous than those at present. At the same time, our data strongly suggest that there is indeed a need to provide training on PrEP to a very large percentage of non-HIV-specialists. On average, this group of respondents had less knowledge and poorer counseling skills with regard to PrEP care, as well as attitudes towards PrEP that were more negative than those reported by HIV-specialists. Non-HIV-specialists in our sample also reported providing pro-active counseling on PrEP to a much smaller proportion of individuals who had an indication for it than did HIV-specialists.

Even if non-HIV-specialists do actively refer patients to PrEP-certified physicians, this still requires them to be able to identify patients with an indication for PrEP and proactively discuss the topic. If the gap between rural and urban areas in Germany (and elsewhere) is to be narrowed in this regard, it will be essential to improve training to these physicians, but to do so in a way that takes better account of the local health infrastructure and geographical barriers, such as long distances to the nearest HIV specialty practices. Online training modules or telemedicine visits are just two options. Certainly, efforts in this direction would be welcomed by the participants in our sample, particularly by the non-HIV-specialists, about 62% of whom indicated that they wished to receive training or information materials on managing PrEP patients. Such training could be augmented by providing the participating physicians with information materials and decision aids for patients in patient-understandable language and in different languages. Indeed, in our survey, decision aids for patients were reported by participating physicians to be the materials they thought would increase the practicability of their PrEP counselling and prescriptions the most. Doing so would be a low-cost and potentially

efficient and effective way to augment the counseling skills of physicians who do not (yet) feel themselves to be competent enough to advice patients on taking PrEP.

There are some interesting similarities between the results of our survey and those of an earlier survey we conducted among counselors in community-based non-governmental STI/HIV counseling centers and local health offices [19]. In the latter, we also found differences in knowledge and attitude scores between the different organizational contexts, with the counseling centers having higher scores in both domains and a much larger proportion of LGBTI+ clientele compared to the local health offices–mirroring in some respects the gaps between HIV-specialists and non-HIV-specialists observed in the present study. Moreover, it is interesting that in the present study, as in our earlier survey, a substantial percentage of participants indicated that it would be helpful to have a clinical practice guideline that contained a clear presentation of indications, contraindications and necessary laboratory tests for PrEP. Given that a guideline on these subjects has, in fact, already been available since 2018, the substantial percentage of participants reporting a wish for such a guideline suggests that the dissemination and implementation of the guideline have been inadequate or that the guideline does not present the relevant information in a clear enough manner.

Limitations

This study has a number of important limitations beyond its observational, cross-sectional design and the obvious caveats that this entails. First, the rate of response to the survey, at 5.53%, was very low. Such response rates are not uncommon in surveys of office-based health professionals, such as GPs or dermato-venereologists, in Europe [21], and knowing this we took extensive efforts to encourage participation in the survey by offering it in different formats and sending email reminders. Nevertheless, the low response rate means that our results are probably not representative of the broader populations of HIV-specialists and non-HIV-specialists in Germany and cannot be easily generalized to them. Along these lines, selection bias is a second potential limitation of this paper. Physicians with either profound or no knowledge of PrEP, and physicians with strongly positive or strongly negative attitudes towards it, may have been more passionate about the subject and therefore more likely to participate. While it is impossible to quantify this bias, it is reasonable to assume that those who were more ambivalent about PrEP were less likely to participate and should therefore be targeted more strongly in any future research of this nature. A third limitation of our study was our use of a self-developed questionnaire that, for pragmatic reasons, did not use validated constructs to measure knowledge and attitudes. There is ample evidence that there often exists a discrepancy between reported knowledge and skills and respondents' actual knowledge and skills [22]. A fourth important limitations is our grouping of MSM and transgender patients for pragmatic purposes, particularly related to the length of the study questionnaire. Differentiating between these two groups would have allowed us to obtain meaningful data on the barriers faced by transgender patients wishing to initiate PrEP, but would have gone beyond the scope of our study. Furthermore, we did not specifically include other populations at risk of acquiring HIV, such as intravenous drug users or sex workers, in our survey in order to increase the participation rate by keeping the questionnaire as short and feasible as possible.

A fifth limitation is our decision not to explore race- or migration-related barriers to PrEP initiation. While a lack of language-relevant materials was listed as a potential barrier and materials in various languages were thought to be helpful by physicians, migrant-specific or race-specific barriers, for example related to discrimination, were not examined. Studies from the US suggest that there are large discrepancies between Black, Indigenous Patients of Color (BIPOC) and white patients with regard to PrEP and antiretroviral uptake [23, 24]. Data on

this subject are sparse, but the discrepancies are likely to be considerable [25]. Given that a substantial proportion of new HIV cases in Germany is among migrants and it is unclear whether the infections have occurred abroad or within Germany [10], it will be crucial in future research to examine structural discriminatory practices that might hamper these individuals' access to appropriate PrEP care. Lastly, the sexual orientation of respondents was not examined in this questionnaire; however, it may play a role in counseling practices, as well as in the choice of whether to specialize in the care of patients living with HIV and of LGBTI + individuals more generally.

Conclusions

The findings of this study on HIV-specialists' and non-HIV-specialists' knowledge of PrEP, their attitudes towards it, and their PrEP counseling practices in Germany point to opportunities to improve PrEP implementation in individuals at risk of acquiring HIV. The large gap between the two groups of physicians with regard to knowledge about and attitudes towards PrEP could be addressed, in part, by providing physicians with patient-centered information material. Online training modules or telemedicine visits may also represent more accessible training options, particularly in rural areas, where few HIV specialists are available. Furthermore, the existing guideline on PrEP should be re-evaluated in terms of its dissemination, implementation and ease of use.

Supporting information

S1 File. Survey questionnaire (Original German version). Original German online version of the questionnaire used in the present survey.
(PDF)

S2 File. Survey questionnaire (English translation). English translation of the online version of the questionnaire used in the present survey. Please note that the present translation has been undertaken for the publication only).
(PDF)

S3 File. Minimal underlying data set and codebook. Age of respondents, postal code, state and qualitative data have been removed to ensure anonymity.
(XLSX)

Author Contributions

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11. Curriculum Vitae

My curriculum vitae does not appear in the electronic version of my paper for reasons of data protection.

12. Complete Publication List

Articles and Abstracts

Sliwinski, S**.; Sammons, M.**; Koca, F.; El youzouri, H.; Vogl, T.; Bechstein, W.O. „A broncho biliary fistula after TACE and microwave ablation of liver metastases of a pancreatic neuroendocrine tumor“. *Zeitschrift für Gastroenterologie*. Submitted 26 January 2023.

Sammons, M.K.; El youzouri, H.; Bechstein, W.O. „Interkuterelle Aspekte der Chirurgie“. *Up2date: Allgemein- und Viszeralchirurgie*. Exepcted Q1 2023.

Sammons, M.K.; Koca, F.; Heise, M.; Bechstein, W.O. A Bronchobiliary Fistula secondary to TACE in a metastatic NET of the pancreas: a case report.” *Deutscher Chirurgen Kongress,* 08 April 2022.

Gaskins, M; **Sammons, M.K.**; Kutscha, F.; Nast, A.; Werner, R.N., „Factors that motivate men who have sex with men in Berlin to use or consider using HIV pre-exposure prophylaxis – A qualitative content analysis of data from a multicentre survey“, *Journal of the International Providers of AIDS Care*, submitted January 2021.

Sammons, M.K.; Gaskins, M.; Kutscha, F.; Nast, A.; Werner, R.N. „HIV Pre-exposure Prophylaxis (PrEP): Knowledge, Attitudes and Counseling Practices among Physicians in Germany – A cross-sectional survey”, *PLoS One*, 16 (4): e0250895. 29 April 2021.

Kutscha, F., Gaskins, M.; **Sammons, M.**; Nast, A.; Werner, R.N., , HIV Pre-Exposure Prophylaxis (PrEP) Counseling in Germany: Knowledge, Attitudes and Practice in Non-governmental and in Public HIV and STI Testing and Counseling Centers. *Frontiers in Public Health*, 2020. 8(298).

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Conference Contributions

“A Bronchobiliary fistula secondary to TACE in a metastatic NET of the pancreas: a case report”. *Deutscher Chirurgen Kongress.* Speaker: **Mary K. Sammons**. Leipzig, Germany. April 06-08.

“Opportunities to improve HIV Pre-Exposure Prophylaxis (PrEP) implementation in persons at risk of acquiring HIV – Results of a survey among physicians in Germany.” Poster Presentation. Deutsch-Österreichischer AIDS-Kongress. Paper-ID: 49998, P9E. 25.-27. März 2021, Online. Speaker: Dr. med. Ricardo N Werner

“Kenntnisse, Einstellungen und Beratungspraxis zur HIV-Präexpositionsprophylaxe (PrEP) unter Ärzt*innen in Deutschland”. STI-Kongress 2020: “STI - wen juckt’s?”. Online Conference, February 2021. Speaker: **Mary K. Sammons**

“HIV Preexposure Prophylaxis (PrEP): Knowledge Attitudes and Advising Practices amongst Physicians

in Germany, 2019". Research Seminar for the Charité's Department of Dermatology, Venerology and Allergology. 17 August 2020. Speaker: **Mary K. Sammons**

„Kenntnisse, Einstellungen und Beratungspraxis zur HIV-Präexpositionsprophylaxe unter Berater*innen in Gesundheitsämtern und in Test- und Beratungsstellen in freier Trägerschaft." *Deutsch-Österreichische AIDS-Konverenz (DOEAK)*. Hamburg, 14.06.2019. Speaker: Dr. med. Ricardo N. Werner

„Kenntnisse und Nutzung der HIV-Präexpositionsprophylaxe. Ergebnisse einer multizentrischen Fragebogenstudie in Berlin unter Männern, die Sex mit Männern haben." Detusche Dermatologische Gesellschaft e.V. (DDG), *Tagung der Deutschen Dermatologischen Gesellschaft (DDG)*. 2019. Speaker: Dr. med. Ricardo N Werner

"Hepatitis B Reactivation in the United States". Speaker: Emmy Ludwig, MD. AASLD Emerging Trends: Hepatitis B Reactivation. Arlington, VA, USA: March 21-22, 2013.

"Incidence and prevalence of hepatitis b virus in an immunosuppressed population". Speaker: **Mary K. Sammons**, Emmy Ludwig. Poster presentation. *Digestive Diseases Week*. Orlando, FL, USA: May 18-21, 2013.

"Incidence and prevalence of hepatitis b virus in an immunosuppressed population". Speaker: **Mary K. Sammons**. Poster presentation. *MSKCC Clinical Research Professionals Week*. New York, NY, USA: June 17-21, 2013.

13. Acknowledgements

I firstly want to thank my doctoral team, Prof. Nast, Dr. Ricardo Werner and Matthew Gaskins, for entrusting me with this project and for challenging me along the way. I have learned a great deal about both research and teamwork, and I am very grateful for the experience. Thank you for the interesting discussions, for challenging me and making me a better scientist.

I would like to thank my first boss and mentor for introducing me to viral research, Dr. Emmy Ludwig; And The Band Played On still sits on my shelf - the research in this dissertation was barely even concevieable at the time of its publication.

A very big thank you to one of my best friends and best personal/scientific advisors, Dr. Jessica Rohmann. Thank you for your open ear, your sound advice, the many cups of coffee and yoga classes.

Thank you to the Sherman family for showing me what perserverance means.

To my favorite lab partner and best friend, Vittoria Criss, thank you for the enlightening discussions in the best of places. I am eternally grateful for our friendship.

Thank you to my mom for always supporting me in my academic pursuits, to New York City and beyond. Thank you for always seeing what I couldn't.

Lastly, thank you to my partner, Toni. I love you and am beyond grateful for all that you do. Thank you for supporting and uplifting me during this entire process.