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Evolution of Massachusetts Physician Attitudes, Knowledge, and Experience Regarding the Use of Antiretrovirals for HIV Prevention

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Abstract

The Center for the AIDS Programme of Research in South Africa (CAPRISA) 004 and Pre-exposure Prophylaxis Initiative (iPrEx) studies demonstrated that topical or oral chemoprophylaxis could decrease HIV transmission. Yet to have an appreciable public health impact, physicians will need to be educated about these new HIV prevention modalities. Massachusetts physicians were recruited via e-mail to complete an online survey of their knowledge and use of HIV prevention interventions. Data were collected before (July–December, 2010) ($n = 178$) and after (December, 2010–April, 2011) ($n = 115$) the release of iPrEx data. Over the two time intervals, knowledge of oral PrEP significantly increased (79% to 92%, $p < 0.01$), whereas knowledge about topical microbicides was already high (89% pre-iPrEx). Post-iPrEx, specialists were more knowledgeable about oral PrEP ($p < 0.01$) and topical microbicides ($p < 0.001$) than generalists. The majority of the respondents would prefer to prescribe topical microbicides (75%) than oral PrEP (25%; $p < 0.001$), primarily because they perceived fewer side effects (95%). Respondents indicated that PrEP should be available if it were a highly effective, daily pill; however, ongoing concerns included: potential drug resistance (93%), decreased funds for other forms of HIV prevention (88%), medication side effects (83%), and limited data regarding PrEP's clinical efficacy (75%). Participants indicated that formal CDC guidelines would have the greatest impact on their willingness to prescribe PrEP (96%). Among Massachusetts physicians sampled, chemoprophylaxis knowledge was high, but current experience was limited. Although topical gel was preferred, responses suggest a willingness to adapt practices pending additional efficacy data and further guidance from normative bodies. Educational programs aimed at incorporating antiretroviral chemoprophylaxis into physicians' HIV prevention practices are warranted.

Introduction

Despite the increasing availability of safe and well-tolerated antiretroviral formulations, almost a quarter million Americans are unaware of their HIV status, and almost 50,000 are newly infected each year.[1] In July 2010, the Center for the AIDS Programme of Research in South Africa (CAPRISA) 004 study established that pericoital administration of 1% tenofovir vaginal gel decreased the risk of HIV acquisition among at-risk heterosexual South African woman.[2] Subsequently, the Pre-exposure Prophylaxis Initiative (iPrEx) study demonstrated that oral antiretroviral pre-exposure prophylaxis (PrEP), with a once-daily tablet containing a fixed dose combination of tenofovir disoproxil fumarate and emtricitabine (FTC-TDF), reduced the risk of HIV acquisition among at-risk men who have sex with men (MSM), compared to a placebo control.[3] While these studies confirm the efficacy of PrEP in clinical trials, they also raise questions about potential challenges to its delivery in real-world settings, in particular, the engagement and training of a cadre of healthcare practitioners to provide PrEP.

Unlike other HIV prevention modalities, PrEP is a biomedical intervention requiring provision by healthcare providers that extends far beyond the administration of medication alone. Providers must also deliver a comprehensive package of preventive care and behavioral interventions to ensure a high rate of adherence and limit risk compensation among PrEP users.[4–7] Thus, clinicians will need to medically

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monitor and encourage frequent HIV testing, as inconsistent use of PrEP could increase the risk of drug resistance among those who acquire HIV while using it.[6,8,9] Providers will also need to be able to communicate the importance of medication adherence and the concept of partial efficacy as adherence is tightly linked to PrEP efficacy,[3] and PrEP may not provide complete protection against HIV acquisition.[4,6,7] Furthermore, to limit the need for indefinite PrEP use by at-risk patients, it will be crucial for providers to counsel PrEP users on sexual risk reduction[3,5,6]—a practice not regularly performed by physicians,[10–14] due to provider discomfort, time constraints, and insufficient training.[13–15]

Despite the necessity for knowledgeable and engaged physicians, to implement PrEP effectively, a dearth of research has assessed providers' interest in PrEP provision or their perceived capacity to deliver the associated package of services. Further, little is known about the extent of providers' knowledge and awareness of PrEP. Thus, in order to implement PrEP safely and effectively, it will be necessary to understand the chemoprophylaxis knowledge, interest, and experience of providers who care for at-risk persons to assess if any unmet educational needs exist among these providers.

The present study used repeated, cross-sectional online surveys to assess the evolution of Massachusetts physicians' knowledge, beliefs, and experience with PrEP before and after the release of iPrEx clinical trial data. Our primary aims were: (1) to evaluate whether specific groups of providers (defined by demographic characteristics, professional training, and experience caring for HIV-infected patients and those at increased risk for HIV) differed in their knowledge, experience, and beliefs regarding the efficacy, prescribing indications, and potential benefits and unintended consequences of PrEP utilization; and (2) to determine whether these constructs changed following the release of iPrEx clinical trial data.[3]

Methods

Participants and procedures

Massachusetts physicians were recruited via professional listserves and direct e-mail to complete an anonymous, online survey before (July–December, 2010) and after (December, 2010–April, 2011) the release of iPrEx trial data. Participants were eligible if they were 18 years of age or older, a licensed medical doctor, worked in Massachusetts, and self-reported as an HIV specialist or generalist. HIV specialists were primarily recruited from the listserves of the Massachusetts membership of the HIV Medical Association (HIVMA) and Infectious Disease Society of America (IDSA). Generalists were primarily recruited via the listserve of the Massachusetts League of Community Health Centers (MLCHC), as well as direct e-mail using hospital, community health center, physician practice group, and university directories from across Massachusetts. The survey was completed by 178 physicians pre-iPrEx and 115 physicians post-iPrEx. With the exception of Duke (Martha's Vineyard) and Nantucket counties, all other Massachusetts counties (12 out of 14) were represented in the pre- and post-iPrEx samples. Survey development was informed by qualitative literature and reports documenting scientific and community stakeholder perceptions regarding the challenges and opportunities associated with PrEP implementation.[16–21] Assessment items were adapted from national consumer and physician surveys[22–24] and prior studies conducted by the Fenway Institute among men who have sex with men.[25–27] The instrument contained 3 domains designed to assess the state of providers knowledge, experiences, and beliefs regarding PrEP before and after the release of iPrEx clinical trial data and differences in these factors by provider type. The 3 domains included: (1) demographics; (2) PrEP-related knowledge, experience, and preferences; and (3) perceived motivators and barriers to PrEP provision. Pre-iPrEx, the survey contained 43 items and required approximately 15–20 min to complete. Post-iPrEx, 16 additional items (not included in the current analyses) were added at the end of the survey, extending the survey by approximately 6 min.

Recruitment e-mails asked providers to share their attitudes, knowledge, and experiences with biomedical and other HIV prevention interventions and contained a hyperlink to a blank copy of the online survey on SurveyMonkey.com.[28] SurveyMonkey.com is a widely used and reputable online survey administration tool and has been found to be acceptable for administering surveys and ensuring participant confidentiality in previously conducted research studies at the Fenway Institute. Upon completion of the survey, participants were redirected to a contact information form where they were given the option to provide their contact information in order to receive a $25 gift card for participating in the study. Participants were informed that their contact information would not be linked to their previously submitted responses or used for nonstudy related purposes.

The study was approved and conducted through the Institutional Review Board (IRB) of Fenway Health in Boston—a freestanding health care and research facility specializing in HIV/AIDS care and serving the needs of the lesbian, gay, bisexual, and transgender people in the greater Boston area.[29]

Measures

Participant characteristics. To assess whether PrEP knowledge, attitudes, and experience differed by provider demographics, we asked participants to report their age, race, medical training, experience caring for HIV-infected patients, personal HIV testing history, and perceived HIV risk. Questions were adapted from Porter Novelli's 2009, National ConsumerStyles©, HealthStyles©, and DocStyles© surveys, developed in conjunction with the U.S. Centers for Disease Control and Prevention (CDC).[22–24]

PrEP-related knowledge, experience, and preferences

Prior to assessing PrEP knowledge, participants were provided with the following statement, "Trials are underway that test whether giving antiretrovirals daily to HIV-uninfected people for months to years will reduce their risk of acquiring HIV infection through ongoing sexual or injection drug use behaviors. This method is called pre-exposure prophylaxis or PrEP." To assess microbicide knowledge, the following statement was provided, "Microbicides are topical coital gels that are being developed to prevent HIV infection. They may contain antiviral drugs." Participants were then asked whether they had heard of oral PrEP and topical microbicides (yes/no).

Participants were also asked to indicate whether they had provided antiretrovirals to HIV-uninfected persons to block infection after an occupational exposure (oPEP or occupational post-exposure prophylaxis), after a sexual or injection drug use nonoccupational exposure (nPEP) and before

anticipated exposure (PrEP). Preference for oral pills or topical microbicides (if comparably efficacious) was dichotomously assessed (microbicides *vs.* pills—oral PrEP). Participants were asked to endorse one or more explanation for their stated preference using a provided list. Additionally, an open-ended response option allowed participants to indicate alternative explanations, not otherwise represented in the list provided.

Motivators and barriers to PrEP provision

Participants were provided with specific hypothetical scenarios (e.g., new efficacy data, recommendations from specific groups or institutions, cost of daily use, and level of efficacy) to examine under which conditions they would feel more comfortable prescribing PrEP. An open-ended response option allowed participants to report any perceived motivators or barriers not otherwise included in the list provided. Questions were adapted from national consumer and physician surveys[22–24] and prior studies conducted through the Fenway Institute.[25–27]

Data analysis

Data from the online surveys were transferred electronically into a database. Participants completing the survey before and after iPrEx were stratified by specialty type (HIV specialist vs. generalist). SAS version 9.2 (Cary, NC) was used to assess sample characteristics and patterns of PrEP knowledge, experience, and preferences, as well as motivators and barriers to PrEP provision. Open-ended responses were analyzed and grouped into categories based on similar themes. To assess statistically significant differences ($p < 0.05$) between groups, OpenEpi was used to conduct chi-square, mid-p exact and t-tests.[30]

Results

Participant characteristics

Participant characteristics, stratified by physician type before and after iPrEx, are depicted in Table 1. The majority of participants were HIV specialists, female, and white, with a mean age of 42 years (SD = 9.8) post-iPrEx. When asked about their sexual behavior in the past 12 months, the majority of participants reported having sex with a partner of the opposite gender; however, about 12% were MSM or women who have sex with women (< 3%).

Only 1% of the sample pre- and post-iPrEx were HIV-infected, with nearly a quarter having been tested for HIV in the past 12 months. Less than 1/5 had never been tested for HIV and most participants described their personal risk of becoming infected as low, despite the majority of both samples knowing someone who was HIV-infected. More of the HIV specialists reported knowing someone with HIV than generalists both pre- (85% specialists; 56% generalists; $p < 0.001$) and post-iPrEx (82% specialists; 65% generalists; $p < 0.05$).

The majority of respondents were trained as internal medicine providers and/or infectious disease providers. Hospitals were the most commonly cited workplace, followed by community health centers. A greater proportion of specialists had cared for HIV- infected MSM, IDU, serodiscordant couples, male or female sex workers, and first responders with frequent exposure to blood/intimate bodily fluids compared to generalists ($p < 0.05$).

PrEP-related knowledge, experience, and preferences

Table 2 presents PrEP knowledge, experiences, and preferences by provider type, before and after the release of the iPrEx results. Over the two time intervals, knowledge of oral PrEP significantly increased (79% to 92%, $p < 0.01$), whereas knowledge about topical microbicides was already high (89% pre-iPrEx). HIV specialists, compared to generalists, tended to be more knowledgeable about oral PrEP and microbicides at both time intervals ($p < 0.01$). The majority of participants (primarily specialists) had prescribed some form of post-exposure prophylaxsis (PEP), however, only 4% had prescribed PrEP post-iPrEx.

Participants generally preferred topical microbicides to oral PrEP ($p < 0.001$) primarily because they perceived fewer side effects (95%). Those who preferred oral PrEP largely believed that it would be easier for patients to use (81%).

Motivators and barriers to PrEP provision

When asked about hypothetical barriers to PrEP provision, the majority of participants cited toxicities in an otherwise healthy population and the development of antiretroviral resistance among PrEP users who become infected (Table 3). Fewer providers were concerned about insufficient/limited data on PrEP clinical efficacy (90% pre-iPrEx; 75% post-iPrEx; $p < 0.001$) and increases in risk behaviors among PrEP users (75% pre-iPrEx; 40% post-iPrEx; $p < 0.001$) post-iPrEx. However, concerns regarding decreased federal funds for other HIV prevention modalities emerged post-iPrEx (33% pre-iPrEx; 88% post-iPrEx; $p < 0.001$).

The major factors that would influence participants' likelihood of prescribing PrEP included formal guidelines from the CDC and requests from patients. Other powerful motivators for PrEP provision included additional clinical efficacy data on MSM, at-risk women, or serodiscordant couples. The providers indicated that recommendations from the CDC, specialty professional associations (e.g., IDSA, HIVMA, etc.), and the US Preventive Services Task Force (USPSTF) would increase their willingness to prescribe PrEP. Post-iPrEx, generalists significantly preferred recommendations from the USPSTF ($p < 0.05$), while HIV specialists significantly preferred recommendations from specialty professional associations (e.g., IDSA, HIVMA etc.; $p < 0.01$).

The majority of participants pre- and post-iPrEx indicated that state health departments or public programs should pay for PrEP if patients could not afford it, with most supporting PrEP at $1.00 per dose. When asked about the efficacy at which providers would feel comfortable prescribing PrEP, participants indicated a mean efficacy level of 71% (SD = 20.4) (post-iPrEx), with no significant differences seen across provider type or time interval. Nearly all of the providers indicated that they would prescribe PrEP if it were a highly effective, once daily pill, with more post-iPrEx generalists than specialists supporting the provision of PrEP as a highly effective twice daily pill ($p < 0.01$).

Discussion

The iPrEx and CAPRISA studies demonstrated that the use of antiretrovirals prior to exposure could help to reduce new HIV infections. Our study is the first to assess providers' knowledge, concerns, and willingness to provide PrEP

Table 1. Demographic Characteristics of Massachusetts Physicians Before (N=178) and After (N=115) Release of iPrEx Clinical Trial Data by Specialty Type

	Pre-iPrEx				*Post-iPrEx*				
	HIV specialist (n=*131*)	*Generalist* (n=*47*)		*Total* (n=*178*)	*Total* (n=*115*)		*HIV specialist* (n=*69*)	*Generalist* (n=*46*)	
	Mean (SD)		*t*			*t*	*Mean (SD)*		*t*
Age in years (*t*)	44 (9.7)	42 (7.8)	*ns*	43 (9.2)	42 (9.8)	*ns*	43 (9.7)	41 (9.9)	*ns*
Year began taking care of HIV-infected persons	1997 (8.9)	1999 (8.9)	*ns*	1997 (8.9)	998 (8.5)	*ns*	1997 (8.4)	1999 (8.4)	*ns*
	% (N)		X^{2h}			X^{2h}	% (N)		X^{2h}
Gender									
Male	47 (61/130)	36 (17/47)	*ns*	44 (78/177)	37 (42/115)	*ns*	41 (28/69)	30 (14/46)	*ns*
Female	53 (69/130)	64 (30/47)		56 (99/177)	63 (73/115)	*ns*	59 (41/69)	70 (32/46)	
Race/ethnicity[a]									
Asian/Asian American/Pacific Islander	16 (21/131)	11 (5/47)	*ns*	15 (26/178)	11 (13/114)	*ns*	13 (9/68)	9 (4/46)	*ns*
Hispanic/Latino/Chicano	6 (8/131)	4 (2/47)	*ns*	6 (10/178)	5 (6/115)	*ns*	7 (5/69)	2 (1/46)	*ns*
African American/black	5 (6/131)	6 (3/47)	*ns*	5 (9/178)	4 (5/115)	*ns*	1 (1/69)	9 (4/46)	*ns*
Caucasian/white	75 (98/131)	81 (38/47)	*ns*	76 (136/178)	77 (89/115)	*ns*	75 (52/69)	80 (37/46)	*ns*
Native American/Alaskan Native	0 (0/131)	0 (0/47)	*ns*	0 (0/178)	1 (1/115)	*ns*	1 (1/69)	0 (0/46)	*ns*
Multiracial	4 (5/131)	0 (0/47)	*ns*	3 (5/178)	3 (3/115)	*ns*	4 (3/69)	0 (0/46)	*ns*
Sexual behavior in past 12 mos									
Male: sex with men	12 (13/109)	13 (5/39)	*ns*	12 (18/148)	9 (8/94)	*ns*	9 (5/58)	8 (3/36)	*ns*
Male: sex with women	37 (40/109)	26 (10/39)	*ns*	34 (50/148)	32 (30/94)	*ns*	36 (21/59)	26 (9/35)	*ns*
Female: sex with men	48 (52/109)	59 (23/39)	*ns*	51 (75/148)	60 (56/94)	*ns*	55 (32/58)	67 (24/36)	*ns*
Female: sex with women	3 (3/109)	3 (1/39)	*ns*	3 (4/148)	1 (1/95)	*ns*	2 (1/59)	0 (0/36)	*ns*
HIV status, testing and personal risk									
Tested for HIV in the past 12 mos	24 (30/126)	24 (11/45)	*ns*	24 (41/171)	23 (25/108)	*ns*	22 (14/65)	26 (11/43)	*ns*
Never tested for HIV	16 (20/126)	11 (5/45)	*ns*	15 (25/171)	16 (17/108)	*ns*	12 (8/65)	21 (9/43)	*ns*
Perceives risk to be low	98 (122/125)	98 (43/44)	*ns*	98 (165/169)	97 (105/108)	*ns*	98 (64/65)	95 (41/43)	*ns*
HIV-infected	1 (1/125)	2 (1/44)	*ns*	1 (2/169)	1 (1/108)	*ns*	0 (0/65)	2 (1/43)	*ns*
Knows someone with HIV	85 (107/126)	56 (25/45)	***16.24***[g]	77 (132/171)	75 (81/108)	*ns*	82 (53/65)	65 (28/43)	***3.72***[e]
Physician type									
HIV specialist	100 (131/131)	0 (0/47)	—	74 (131/178)	59 (69/115)	***5.96***[f]	100 (69/69)	0 (0/46)	—
Generalist	0 (0/131)	100 (47/47)	—	26 (47/178)	51 (46/115)	*ns*	0 (0/69)	100 (46/46)	—
Physician training[a]									
Internal medicine	85 (111/131)	43 (20/47)	***31.67***[g]	74 (131/178)	76 (87/115)	*ns*	81 (56/69)	67 (31/46)	*ns*
Infectious disease	78 (102/131)	0 (0/47)	[g,h]	57 (102/178)	46 (53/115)	*ns*	77 (53/69)	0 (0/46)	[g,h]
Family medicine	2 (3/131)	28 (13/47)	[g,h]	9 (16/178)	10 (11/115)	*ns*	4 (3/69)	17 (8/46)	[e,h]
Pediatrics	6 (8/131)	32 (15/47)	***20.48***[g]	13 (23/178)	11 (13/115)	*ns*	9 (6/69)	15 (7/46)	*ns*
Obstetrics and gynecology	2 (2/131)	2 (1/47)	*ns*	2 (3/178)	2 (2/115)	*ns*	1 (1/69)	2 (1/46)	*ns*
Psychiatry	2 (3/131)	0 (0/47)	*ns*	2 (3/178)	2 (2/115)	*ns*	3 (2/69)	0 (0/46)	*ns*
Other[b]	2 (3/131)	2 (1/47)	*ns*	2 (4/178)	3 (4/115)	*ns*	1 (1/69)	7 (3/46)	*ns*

(*continued*)

Table 1. (Continued)

	Pre-iPrEx				*Post-iPrEx*				
	HIV specialist (n=*131*)	*Generalist* (n=*47*)		*Total* (n=*178*)	*Total* (n=*115*)		*HIV specialist* (n=*69*)	*Generalist* (n=*46*)	
	Mean (SD)		*t*			*t*	*Mean (SD)*		*t*
Workplace[a]									
Community health center	17 (22/130)	77 (36/47)		33 (58/177)	36 (41/115)	*ns*	23 (16/69)	54 (25/46)	
Hospital	70 (91/130)	17 (8/47)		56 (99/177)	53 (61/115)	*ns*	65 (45/69)	35 (16/46)	
Physician practice group	9 (12/130)	6 (3/47)		9 (15/177)	8 (9/115)	*ns*	7 (5/69)	9 (4/46)	
Independent practice group	0 (0/130)	0 (0/47)		0 (0/177)	2 (2/115)	*ns*	1 (1/69)	2 (1/46)	
AIDS service organization	1 (1/130)	0 (0/47)	***56.97***[g]	1 (1/177)	2 (2/115)	*ns*	3 (2/69)	0 (0/46)	***13.83***[f]
Health department	2 (2/130)	0 (0/47)		1 (2/177)	0 (0/115)	*ns*	0 (0/69)	0 (0/46)	
Academic	1 (1/130)	0 (0/47)		1 (1/177)	0 (0/115)	*ns*	0 (0/69)	0 (0/46)	
Corporation	1 (1/130)	0 (0/47)		1 (1/177)	0 (0/115)	*ns*	0 (0/69)	0 (0/46)	
Number of HIV-infected persons ever treated									
0	0 (0/131)	17 (8/47)		5 (8/178)	2 (2/115)	*ns*	0 (0/69)	4 (2/46)	
1–5	0 (0/131)	19 (9/47)		5 (9/178)	10 (12/115)	*ns*	1 (1/69)	24 (11/46)	
5–20	1 (1/131)	26 (12/47)		7 (13/178)	12 (14/115)	*ns*	3 (2/69)	26 (12/46)	
20–50	14 (18/131)	23 (11/47)	***104.96***[g]	16 (29/178)	14 (16/115)	*ns*	7 (5/69)	24 (11/46)	***59.51***[g]
50–100	15 (20/131)	6 (3/47)		13 (23/178)	21 (24/115)	*ns*	23 (16/69)	17 (8/46)	
100 or more	70 (92/131)	9 (4/47)		54 (96/178)	41 (47/115)	***4.77***[e]	65 (45/69)	4 (2/46)	
Cared for HIV-infected persons[a]									
MSM[c]	96 (124/129)	68 (27/40)	***26.29***[g]	89 (151/169)	91 (101/111)	*ns*	96 (65/68)	84 (36/43)	***4.53***[e]
IDU[d]	95 (123/129)	76 (31/41)	***14.22***[g]	91 (154/170)	93 (104/112)	*ns*	97 (67/69)	86 (37/43)	***4.88***[e]
Serodiscordant couples	87 (112/129)	55 (22/40)	***18.83***[g]	79 (134/169)	74 (82/111)	*ns*	83 (57/69)	60 (25/42)	***7.21***[f]
Sex workers (male or female)	69 (87/127)	25 (9/36)	***21.93***[g]	59 (96/163)	46 (51/111)	***4.45***[e]	58 (40/69)	26 (11/42)	***10.62***[g]
First responders with frequent exposure to blood/intimate bodily fluids	60 (76/127)	16 (6/37)	***21.81***[g]	50 (82/164)	43 (47/110)	*ns*	59 (40/68)	17 (7/42)	***18.86***[g]

[a]Participants checked all that applied. Percentages may exceed 100%.
[b]Other specialties include emergency, preventative, gastrointestinal, and adolescent medicine.
[c]MSM, men who have sex with men; [d]IDU, injection drug users.
[e]$p<0.05$; [f]$p<0.01$; [g]$p<0.001$; [h]Mid P exact tests used where cell counts were <5.
Note: Percentages may exceed 100% due to rounding.

Table 2. PrEP Knowledge, Experience, and Preferences Among Massachusetts Physicians Before (n=178) and After (*n*=115) Release of iPrEx Clinical Trial Data by Specialty Type

	Pre-iPrEx				*Post-iPrEx*				
	HIV specialist (n=*131*)	*Generalist* (n=*47*)		*Total* (n=*178*)	*Total* (n=*115*)		*HIV specialist* (n=*69*)	*Generalist* (n=*46*)	
	% (*N*)		X^{2+}			X^{2+}	% (*N*)		X^{2+}
PrEP knowledge									
Heard of PrEP	95 (121/128)	36 (17/47)	***70.23***[e]	79 (138/175)	92 (105/114)	***9.05***[d]	99 (67/68)	83 (38/46)	***9.56***[d]
Heard of topical microbicides	100 (127/127)	57 (27/47)	***20.99***[e]	89 (154/174)	83 (94/113)	*ns*	96 (65/68)	64 (29/45)	***18.78***[e]
Past provision of antiretrovirals to prevent HIV transmission[a]									
No	20 (26/129)	60 (28/47)	***23.18***[e]	31 (54/176)	38 (43/113)	*ns*	16 (11/68)	71 (32/45)	***34.67***[e]
Yes, after an occupational exposure (PEP or post-exposure prophylaxis)	78 (100/129)	30 (14/47)	***34.40***[e]	65 (114/176)	58 (66/113)	*ns*	81 (55/68)	24 (11/45)	***35.51***[e]
Yes, after a sexual or injection drug use nonoccupational exposure (nPEP)	55 (71/129)	19 (9/47)	***17.90***[e]	45 (80/176)	46 (52/113)	*ns*	68 (46/68)	13 (6/45)	***32.16***[e]
Yes, before anticipated exposure(s) (PrEP)	9 (11/129)	2 (1/47)	*ns*	7 (12/176)	4 (5/113)	*ns*	7 (5/68)	0 (0/45)	*ns*
Preference for oral PrEP vs. topical gel									
Prefer oral PrEP	32 (41/127)	22 (10/46)	*ns*	29 (51/173)	25 (27/106)	*ns*	24 (15/63)	28 (12/43)	*ns*
Prefer topical microbicides	68 (86/127)	78 (36/46)	*ns*	71 (122/173)	75 (79/106)	*ns*	76 (48/63)	72 (31/43)	*ns*
Beliefs dictating oral PrEP preference[a]									
Pill could be easier to take	90 (37/41)	90 (9/10)	*ns*	90 (46/51)	81 (22/27)	*ns*	80 (12/15)	83 (10/12)	*ns*
Pill could be less stigmatizing than gel, since many people take medication	59 (24/41)	40 (4/10)	*ns*	55 (28/51)	48 (13/27)	*ns*	60 (9/15)	33 (4/12)	*ns*
Pill could be cheaper	20 (8/41)	20 (2/10)	*ns*	20 (10/51)	7 (2/27)	*ns*	13 (2/15)	0 (0/12)	*ns*
Pill could have fewer side effects	10 (4/41)	10 (1/10)	*ns*	10 (5/51)	4 (1/27)	*ns*	7 (1/15)	0 (0/12)	*ns*
Pill: other[b]	22 (9/41)	3 (3/10)	*ns*	24 (12/51)	19 (5/27)	*ns*	20 (3/15)	17 (2/12)	*ns*
Pill can be used for any type of exposure	33 (3/9)	33 (1/3)	*ns*	33 (4/12)	20 (1/5)	*ns*	33 (1/3)	0 (0/2)	*ns*
Patients likely to find pill more acceptable	22 (2/9)	33 (1/3)	*ns*	25 (3/12)	80 (4/5)	*ns*	67 (2/3)	100 (2/2)	*ns*
Patients may be more adherent with pill	22 (2/9)	0 (0/3)	*ns*	17 (2/12)	0 (0/5)	*ns*	0 (0/3)	0 (0/3)	*ns*
Pill likely to be more effective than gel	11 (1/9)	33 (1/3)	*ns*	17 (2/12)	0 (0/5)	*ns*	0 (0/3)	0 (0/3)	*ns*
Pill allows for proper dosing	11 (1/9)	0 (0/3)	*ns*	8 (1/12)	0 (0/5)	*ns*	0 (0/3)	0 (0/3)	*ns*
Beliefs dictating topical gel preference[a]									
Gel could have fewer side effects	91 (78/86)	94 (34/36)	*ns*	92 (112/122)	95 (75/79)	*ns*	96 (46/48)	94 (29/31)	*ns*
Gel could be easier to use	60 (52/86)	72 (26/36)	*ns*	64 (78/122)	56 (44/78)	*ns*	53 (25/47)	61 (19/31)	*ns*
Many people already use lubricants for sex	51 (44/86)	64 (23/36)	*ns*	55 (67/122)	52 (41/79)	*ns*	52 (25/48)	52 (16/31)	*ns*
Gel could be cheaper	47 (40/86)	44 (16/36)	*ns*	46 (56/122)	52 (41/79)	*ns*	54 (26/48)	48 (15/31)	*ns*
Gel could be less stigmatizing than taking medication	43 (37/86)	47 (17/36)	*ns*	44 (54/122)	39 (31/79)	*ns*	40 (19/48)	39 (12/31)	*ns*
Gel: other[b]	26 (22/86)	14 (5/36)	*ns*	22 (27/122)	28 (22/79)	*ns*	31 (15/48)	23 (7/31)	*ns*
Less risk of drug resistance due to local absorption	82 (18/22)	40 (2/5)	*ns*	74 (20/27)	64 (14/22)	*ns*	6 (9/15)	71 (5/7)	*ns*
Patients may be more adherent due to episodic use	5 (1/22)	40 (2/5)	*ns*	11 (3/27)	27 (6/22)	*ns*	27 (4/15)	29 (2/7)	*ns*
Empowerment of receptive partner	14 (3/22)	0 (0/5)	*ns*	7 (2/27)	0 (0/22)	*ns*	0 (0/15)	0 (0/7)	*ns*
Prefer gel, but would offer patients the choice	0 (0/22)	20 (1/5)	*ns*	4 (1/27)	9 (2/22)	*ns*	13 (2/15)	0 (0/7)	*ns*

[a]Participants checked all that applied. Percentages may exceed 100%.
[b]Participants indicated a response not otherwise provided. Items under "other" are based on themes derived from open-ended responses.
[c]$p<0.05$; [d]$p<0.01$; [e]$p<0.001$; [f]Mid P exact tests used where cell counts were <5.
Note: Percentages may exceed 100% due to rounding.

Table 3. Motivators and Barriers to PrEP Provision Among Massachusetts Area Physicians Before (N = 178) and After (*N* = 115) Release of iPrEx Clinical Trial Data by Specialty Type

	Pre-iPrEx				*Post-iPrEx*				
	HIV specialist (N = *131*)	*Generalist* (N = *47*)		*Total* (N = *178*)	*Total* (N = *115*)		*HIV specialist* (N = *69*)	*Generalist* (N = *46*)	
	Mean (SD)		*t*			*t*	*Mean (SD)*		*t*
Desired % efficacy to RX PrEP	75 (19.2)	74 (22.3)	ns	75 (20.0)	71 (20.4)	ns	70.8 (18.5)	71.3 (23.1)	*ns*
	% (N)		X^{2g}			X^{2g}	% (N)		X^{2g}
Hypothetical barriers to PrEP provision[a]									
Toxicities in an otherwise healthy population	91 (115/127)	89 (42/47)	*ns*	90 (157/174)	83 (91/110)	*ns*	79 (53/67)	88 (38/43)	*ns*
Limited data on PrEP's clinical efficacy	89 (113/127)	91 (43/47)	*ns*	90 (156/174)	75 (82/110)	***11.34***[f]	76 (51/67)	72 (31/43)	*ns*
Development of antiretroviral resistance among PrEP users	89 (113/127)	89 (42/47)	*ns*	89 (155/174)	94 (103/110)	*ns*	97 (65/67)	88 (38/43)	*ns*
Increases in risk behaviors among PrEP users	78 (99/127)	66 (31/47)	*ns*	75 (130/174)	40 (44/110)	***34.22***[f]	45 (30/67)	33 (14/43)	*ns*
Insufficient federal funds to support the cost PrEP	31 (40/127)	49 (23/47)	***4.52***[d]	36 (63/174)	26 (29/110)	*ns*	30 (20/67)	21 (9/43)	*ns*
Decrease in federal funds for other HIV prevention modalities	35 (44/127)	30 (14/47)	*ns*	33 (58/174)	88 (97/110)	***81.78***[f]	87 (58/67)	91 (39/43)	*ns*
Time associated with clinical monitoring	15 (19/127)	15 (7/47)	*ns*	15 (26/174)	15 (17/110)	*ns*	10 (7/67)	23 (10/43)	*ns*
Time required to provide counseling and prevention education	12 (15/127)	6 (3/47)	*ns*	10 (18/174)	11 (12/110)	*ns*	6 (4/67)	19 (8/43)	[d,g]
Community backlash	6 (8/127)	15 (7/47)	*ns*	9 (15/174)	6 (7/110)	*ns*	6 (4/67)	7 (3/43)	*ns*
Other[c]	6 (2/127)	0 (0/47)	*ns*	1 (2/174)	0 (0/110)	*ns*	0 (0/67)	0 (0/73)	*ns*
Challenges likely to vary by patient/population	100 (2/2)	0 (0/0)	*ns*	100 (2/2)	0 (0/0)	*ns*	0 (0/0)	0 (0/0)	*ns*
Hypothetical motivators for PrEP provision[a]									
New information:									
Additional clinical efficacy data about MSM	87 (111/127)	81 (38/47)	*ns*	86 (149/174)	83 (91/110)	*ns*	82 (54/66)	84 (37/44)	*ns*
Additional clinical efficacy data about at-risk women	89 (113/127)	83 (39/47)	*ns*	87 (152/174)	81 (90/111)	*ns*	82 (55/67)	80 (35/44)	*ns*
Additional clinical efficacy data about HIV discordant couples	90 (114/127)	85 (40/47)	*ns*	89 (154/174)	78 (87/111)	***5.32***[d]	79 (53/67)	77 (34/44)	*ns*
CDC or Public Health Service guidelines	96 (122/127)	98 (46/47)	*ns*	97 (168/174)	96 (106/110)	*ns*	98 (65/66)	93 (41/44)	*ns*
State or local public health department guidelines	54 (69/127)	83 (39/47)	***11.96***[f]	62 (108/174)	58 (64/110)	*ns*	56 (37/66)	61 (27/44)	*ns*
Successful clinical monitoring outcomes	59 (75/127)	68 (32/47)	*ns*	61 (107/174)	66 (73/110)	*ns*	61 (40/66)	75 (33/44)	*ns*
Request from patient	94 (117/124)	98 (45/46)	*ns*	95 (162/170)	92 (102/111)	*ns*	88 (59/67)	98 (43/44)	*ns*
Recommendations from:									
CDC	81 (103/127)	87 (41/47)	*ns*	83 (144/174)	86 (95/111)	*ns*	84 (56/67)	89 (39/44)	*ns*
US preventive services task force	72 (91/127)	87 (41/47)	***4.55***[d]	76 (132/174)	73 (80/110)	*ns*	65 (43/66)	84 (37/44)	***4.77***[d]
National medical association (e.g., AMA, NMA, etc.)	37 (47/127)	57 (27/47)	**5.86**[d]	43 (74/174)	40 (44/110)	*ns*	39 (26/66)	41 (18/44)	*ns*
Specialty professional association (e.g., IDSA, HIVMA, etc.)	88 (112/127)	57 (27/47)	**20.18**[f]	80 (139/174)	85 (94/110)	*ns*	94 (62/66)	73 (32/44)	**9.56**[e]
Organizational practice statements (e.g., HMO, VA, etc.)	16 (20/127)	30 (14/47)	**4.30**[d]	20 (34/174)	17 (19/110)	*ns*	14 (9/66)	23 (10/44)	*ns*
Third party payers	12 (15/127)	19 (9/47)	*ns*	14 (24/174)	18 (20/111)	*ns*	15 (10/67)	23 (10/44)	*ns*
Fellow providers	37 (47/127)	47 (22/47)	*ns*	40 (69/174)	43 (48/111)	*ns*	42 (28/67)	46 (20/44)	*ns*
Patients who have used PrEP	35 (44/127)	49 (23/47)	*ns*	39 (67/174)	34 (38/111)	*ns*	31 (21/67)	39 (17/44)	*ns*
Other[c]	7 (3/44)	9 (2/23)	*ns*	3 (5/174)	5 (6/111)	*ns*	6 (4/67)	5 (2/44)	*ns*

(*continued*)

Table 3. (Continued)

	Pre-iPrEx				*Post-iPrEx*				
	HIV specialist (N=131)	*Generalist (N=47)*		*Total (N=178)*	*Total (N=115)*		*HIV specialist (N=69)*	*Generalist (N=46)*	
	Mean (SD)		*t*			*t*	*Mean (SD)*		*t*
National/international organizations (WHO, UNAIDS, FDA, DHHS)	66 (2/3)	50 (1/2)	*ns*	60 (3/5)	50 (3/6)	*ns*	75 (3/4)	0 (0/2)	*ns*
Community initiatives supporting use/standards of care	33 (1/3)	50 (1/2)	*ns*	40 (2/5)	0 (0/6)	*ns*	0 (0/4)	0 (0/2)	*ns*
Insurance coverage	0 (0/3)	0 (0/2)	*ns*	0 (0/5)	50 (3/6)	*ns*	25 (1/4)	100 (2/2)	*ns*
Government subsidy of PrEP									
State health departments/public programs should pay for PrEP if patients cannot afford it	80 (97/122)	83 (39/47)	*ns*	80 (136/169)	73 (82/112)	*ns*	72 (49/68)	75 (33/44)	*ns*
Cost-based recommendation[b]									
0.10¢ per use	16 (19/122)	22 (10/46)	*ns*	17 (29/168)	8 (9/109)	***4.53***[d]	6 (4/67)	12 (5/42)	*ns*
0.50¢ per use	25 (31/122)	20 (9/46)	*ns*	24 (40/168)	25 (27/109)	*ns*	21 (14/67)	31 (13/42)	*ns*
$1.00 per use	39 (48/122)	48 (22/46)	*ns*	42 (70/168)	55 (60/109)	***4.75***[d]	55 (37/67)	55 (23/42)	*ns*
$5.00 per use	14 (17/122)	4 (2/46)	*ns*	11 (19/168)	9 (10/109)	*ns*	13 (9/67)	2 (1/42)	ns
I would not recommend PrEP for daily use at any price	6 (7/122)	7 (3/46)	*ns*	7 (11/168)	3 (3/109)	*ns*	5 (3/67)	0 (0/42)	*ns*
Conditional provision of PrEP									
If it were a highly effective, once-daily pill	94 (112/119)	100 (42/42)	*ns*	96 (154/161)	95 (103/108)	*ns*	94 (61/65)	98 (42/43)	*ns*
If it were a highly effective, twice-daily pill	63 (71/113)	88 (37/42)	**9.25**[e]	70 (108/155)	63 (67/106)	*ns*	51 (32/63)	81 (35/43)	***10.29***[f]

[a]Participants were asked to check all that apply. Percentages may exceed 100%.
[b]Cost at which physician would recommend PrEP for daily use.
[c]Participants indicated a response not otherwise provided. Items under "other" are based on themes derived from open-ended responses.
[d]$p < 0.05$; [e]$p < 0.01$; [f]$p < 0.001$.
[g]Mid P exact tests used where cell counts were < 5.
Note: Percentages may exceed 100% due to rounding.

following the release of the iPrEx trial data. Among this sample of Massachusetts area physicians, knowledge of topical and oral chemoprophylaxis was high—92% had heard of oral PrEP and 83% had heard about topical microbicides, post-iPrEx. Yet despite nearly 60% having previously prescribed some form of PEP, only 4% of the sample had prescribed PrEP post-iPrEx. Not surprisingly, HIV specialists had significantly more knowledge ($p < 0.01$) and experience ($p < 0.001$) providing antiretrovirals for prevention, compared to generalists, although PrEP provision remained limited among specialists (7% post-iPrEx). While Massachusetts physicians overwhelmingly indicated a preference for topical microbicides, primarily due to perceptions that gels would have fewer side effects than oral medication, those who preferred oral PrEP predominantly felt that it would be easier to take. These responses suggest a willingness to prescribe PrEP pending the availability of new efficacy data and further guidance from normative bodies.

As with any new treatment or intervention, uptake can be slow, and barred by both real and hypothetical concerns regarding the consequences of increased availability and delivery of the treatment. Community and scientific stakeholders have expressed ongoing concerns that widespread PrEP availability could lead to increases in sexual risk-taking among PrEP users (risk compensation).[4–6,9,17,20] Providers in this study tended to express these concerns before the release of iPrEx clinical trial data, however, concerns decreased post-iPrEx. This suggests an awareness of the iPrEx results which did not find evidence of risk compensation among study participants.[3] Instead, providers expressed increased funding concerns post-iPrEx (i.e., that the availability of PrEP would lead to decreases in available federal funds for other forms of HIV prevention and treatment). Nonetheless, providers indicated that they would support the provision of PrEP if modestly priced at $1.00 per use, with the majority of the post-iPrEx sample (73%) indicating that state health departments or public programs should pay for PrEP if patients cannot afford to pay for it themselves. This could present future challenges for implementing oral PrEP with tenofovir-emtirictabine, since the cost of this agent in the U.S. and other resource-rich nations is more than 100 times that price point.[18,31–33]

While concerns relating to PrEP's clinical efficacy declined post-iPrEx, providers noted that additional clinically efficacy data on at-risk persons could motivate them to prescribe PrEP, with providers on average supporting the provision of PrEP at an efficacy level of 71%. In fact, if proven highly effective, the majority of providers (95%) indicated that they would prescribe PrEP if it were a once daily pill. Given this result, an important consideration when educating providers will be to accurately convey the relationship between adherence and increasing partial efficacy that has been observed in several completed PrEP trials. For example, the overall efficacy of PrEP has ranged from 39% in CAPRISA 004 (with a topical formulation used pericoitally by African women) to 73% in the Partners PrEP study (with daily oral PrEP used by the HIV-uninfected members of serodiscordant heterosexual couples), but among subgroups of participants with excellent adherence in several studies, PrEP efficacy estimates have reached the 90% range.[2,3,34,35] Additionally, fears relating to PrEP's potential unintended consequences could potentially act as a barrier to future PrEP provision as many providers expressed concerns about the development of antiretroviral resistance among PrEP users who become HIV-infected. Since efficacy is highly tied to medication adherence, it will be necessary to train providers in communicating concepts of adherence and partial efficacy, in addition to providing clinical monitoring—a time constraint more commonly cited by generalists than specialists.

Although the CDC released interim PrEP guidance in January 2011,[36] the post-iPrEx sample indicated that further guidance from the CDC and other normative bodies could motivate them to prescribe PrEP. HIV specialists tended to place greater value on recommendations from specialty professional associations (e.g., IDSA, HIVMA etc.), while more generalists indicated that recommendations from the US Preventive Services Task Force could motivate them to prescribe PrEP in the future. Requests from patients were also cited as potential motivators for PrEP provision. Given recent data demonstrating a substantial interest in PrEP among at-risk MSM,[37] it will be important for providers to make PrEP available to patients who could benefit from its use. However, research indicates that sexual risk taking histories are not routinely assessed in HIV or primary care settings due to provider time constraints, discomfort, lack of motivation and other barriers,[11–15] making it potentially difficult for providers to identify appropriate candidates for PrEP use. Thus, future professional educational campaigns should not only aim to increase provider knowledge of PrEP and its appropriate provision, but also address provider barriers to allow for the integration of routine sexual risk inventories into medical care.

Some study limitations should be noted. First, our study used professional listserves and direct e-mail in recruiting providers to complete an anonymous, online survey before and after the release of iPrEx clinical trial data. Due to the anonymous nature of the survey, we were not able to track participant responses across surveys. Thus, unlike traditional repeat cross-sectional designs, it is likely that some of the individuals who completed the post-iPrEx survey, did not complete the pre-iPrEx survey, and vice versa. As a result of this limitation, the data of providers who completed both surveys may be biased toward greater knowledge and more amenable attitudes toward PrEP post-iPrEx. However, it is more plausible that the addition of new participants post-iPrEx served to skew the data in the other direction, as slight (not statistically significant) decreases were seen in microbicide knowledge post-iPrEx. Nonetheless, the demographic make-up of the two samples were similar with the exception of fewer HIV specialists, and thus fewer providers who had cared for specific subsets of HIV- infected persons in the post-iPrEx sample. Next, the recruitment lists were not exhaustive and may not have included all HIV specialists and generalists practicing in Massachusetts. Because of limited funding, this study was conducted with Massachusetts physicians only, and as such, our findings may not be fully generalizable to medical providers across the U.S. Finally, the results of this study are based on the PrEP-related knowledge, experience, and beliefs of Massachusetts physicians almost immediately post-iPrEx and may change over time as new information becomes available.

These findings warrant the development of educational programs aimed at incorporating antiretroviral chemoprophylaxis into physicians' HIV prevention practices. Such programs should take into account the range of professional

education needs, addressing differences in PrEP awareness by provider specialty, concerns regarding the potential outcomes of PrEP, as well as the willingness and ability to effectively deliver PrEP and its associated package of comprehensive services.

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