Correlates of lower comprehension of informed consent among participants enrolled in a cohort study in Pune, India

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Background: Optimum comprehension of informed consent by research participants is essential yet challenging. This study explored correlates of lower comprehension of informed consent among 1334 participants of a cohort study aimed at estimating HIV incidence in Pune, India.

Methods: As part of the informed consent process, a structured comprehension tool was administered to study participants. Participants scoring $\geq 90\%$ were categorised into the 'optimal comprehension group', whilst those scoring 80–89% were categorised into the 'lower comprehension group'. Data were analysed to identify socio-demographic and behavioural correlates of lower consent comprehension.

Results: The mean $\pm$ SD comprehension score was $94.4 \pm 5.00\%$. Information pertaining to study-related risks was not comprehended by 61.7% of participants. HIV-negative men (adjusted OR [AOR] = 4.36, 95% CI 1.71–11.05) or HIV-negative women (AOR = 13.54, 95% CI 6.42–28.55), illiteracy (AOR = 1.65, 95% CI 1.19–2.30), those with a history of multiple partners (AOR = 1.73, 95% CI 1.12–2.66) and those never using condoms (AOR = 1.35, 95% CI 1.01–1.82) were more likely to have lower consent comprehension.

Conclusions: We recommend exploration of domains of lower consent comprehension using a validated consent comprehension tool. Improved education in these specific domains would optimise consent comprehension among research participants.

Keywords: Informed consent process, Comprehension, Consent comprehension tool, Illiteracy, Study related risks, India

Introduction

Respect for individuals, beneficence and justice form the ethical framework of research involving human subjects. Respect for persons entails that any potential research participant should be given the opportunity to make an informed choice about his/her participation in the research. To enable individuals to make this choice, research participants should have adequate comprehension of the research based on complete information given by the researchers. This opportunity is provided through an appropriate informed consent process.¹ Adequate informed consent has three primary constituents: information; comprehension; and voluntary decision. Obtaining informed consent is a challenge especially in developing countries primarily due to low levels of literacy in the communities as well as inadequate sensitisation about the practice of research ethics among researchers.² This often leads to inadequate understanding of complex scientific terms by the research participants.^{3,4} Indian Ethical Guidelines for Biomedical Research on Human Participants have also

emphasised the importance of informed consent and recognised the challenge of ensuring compliance with the ethical principle of 'do no harm'.⁵ The guidelines recommend pursuance of 12 general principles to ensure ethical conduct of any human subject research in India, and informed consent is an integral part of those guidelines. To make the informed consent process more meaningful, it is recommended that researchers should be particularly vigilant in the case of vulnerable populations. They should ensure that there is no therapeutic misconception among potential research participants, especially among socially disadvantaged populations in developing countries.⁶

Comprehension of the informed consent form facilitates a coercion-free as well as informed decision regarding research participation by potential participants. To enhance consent comprehension, researchers have employed a variety of interventions. These include use of non-technical language in the informed consent forms,⁷ simpler vocabulary,⁸ improving readability,⁹ using visual aids,¹⁰ developing a tool for assessment of understanding^{11–13} and providing adequate time for the

informed consent process. Despite these efforts, certain challenges during comprehension of informed consent were evident from studies conducted in developing countries. The reported concerns include lower comprehension of study-related risks,¹⁴ study background¹³ and the side effects of experimental drugs.¹⁵ It is important to identify the aspects that are not understood by potential research participants with the help of a comprehension tool. Comprehension is not only gaining knowledge but making appropriate decisions based on that knowledge. Hence, participants' comprehension can be assessed by presenting anecdotal situations and seeking answers from the participants. While answering, participants would then require applying the knowledge gained during the consent process. Comprehension tools comprise of qualitative and quantitative assessments. Quantitative comprehension tools are easier to implement as they are simple to administer, more objective in evaluation and require only a modest level of staff training.¹⁶ Basic demographic characteristics such as literacy and cultural background have been reported to affect consent comprehension in a study conducted in the USA.¹⁷ In an Indian study on comprehension of pre-surgical informed consent, it was observed that older, less educated and poorer patients performed worse than the others.¹⁸ Besides having an appropriate tool for comprehension assessment, researchers have also indicated the need to identify the impact of sociodemographic factors, cultural norms and attitudes on the quality of the informed consent process.¹⁹ A consent comprehension questionnaire was developed for participants enrolled in a clinical trial preparedness study aimed at determining the incidence of HIV infection among a high-risk population in Pune, India. Various dimensions of lower comprehension of informed consent and its correlates were assessed among these study participants.

Methods

The study was conducted by the National AIDS Research Institute (NARI) (Pune, India) in collaboration with the School of Medicine of Johns Hopkins University (Baltimore, MD, USA). After obtaining informed consent, 1337 individuals (457 HIV-discordant couples and 423 HIV-uninfected women) were enrolled in a prospective cohort study between September 2002 and December 2004. The study was aimed at determining the incidence of HIV-1 infection. Demographic and clinical data were collected at quarterly follow-up visits. Clinical procedures in the study consisted of pre-test and post-test counselling, clinical examination, appropriate treatment, and monitoring of CD4 count and viral load every 3 months and 6 months, respectively, for HIV-infected individuals identified during implementation of the study. Study participants were clinically evaluated by the physicians during all follow-up visits and also during unscheduled interim visits whenever required. Study participants requiring inpatient care were admitted to two pre-identified local hospitals and were jointly managed by the study and hospital physicians. The clinical procedures for HIV-uninfected participants involved quarterly HIV counselling and testing as well as physical examination and provision of required standard care. Detailed methodology including various clinical procedures and important research findings of this study have been described in previous papers.^{20, 21}

Participant recruitment

Study participants were recruited from the Community Involvement Plan (CIP) of NARI, especially designed to impart research literacy to the community and to ensure community engagement in research. The CIP mechanism was used to provide information about the study as well as risks and benefits of participation to potential study participants in the community. Interested individuals were referred to the NARI study clinics for recruitment into the study. In addition, participants were also recruited from patients using the voluntary counselling and testing service at various NARI clinics. During the recruitment procedure, potentially eligible participants were given complete information about the study in a one-to-one session with a trained counsellor or community educator.

Informed consent process

Informed consent forms for the study were originally developed in the English language and their translated versions in the local language were used during the informed consent process of the study. Accuracy of the translations was ensured by back-translating the translated version by a person not involved in the study and matching the same with the original template.

A two-step informed consent process was used in the study. In step 1, screening of potential participants was done to establish eligibility for the study using the screening consent form. Sexually active HIV-uninfected women aged ≥ 18 years reporting to the sexually transmitted infections clinic constituted one component of the female cohort. Sexually active HIV serodiscordant couples where both the partners were aged ≥ 18 years and where the HIV-infected partner's status was known to the other partner were eligible to participate. In the couples' setting, HIV-infected men and HIV-uninfected partners of HIV-infected women formed the male cohort. HIV-infected women and HIV-uninfected partners of HIV-infected men formed the second component of the female cohort.

In step 2, participants found to be eligible in the screening evaluation were administered enrolment informed consent by the study counsellors. The enrolment informed consent form explained study enrolment and follow-up procedures in detail. It emphasised the fact that they were participating in research. It also explained the purpose of conducting the study as well as study procedures such as obtaining blood samples for HIV testing, physical examination for sexually transmitted infection diagnosis, and administering a questionnaire for obtaining behavioural information. The consent form provided information regarding the possibility of discomfort during the physical examination, sample collection, and social harms because of breach of confidentiality and marital discord resulting from the HIV discordant relationship. The benefits such as quarterly HIV testing for HIV-uninfected participants, quarterly CD4 tests for the HIV-infected partner, and primary care and referral services were mentioned in the informed consent form. Study participants were ensured that their participation was entirely voluntary and participants had a right to withdraw their participation any time during the study without losing the benefits of care provided in the study clinics. Informed consent also provided assurance of confidentiality and information on storage of leftover blood samples. Participants' queries were answered

during discussion of the informed consent with the respective counsellors. Subsequently, a test of comprehension or understanding, which was a structured questionnaire, was administered to participants by the study clinic staff members, who were not directly involved in consent, counselling, recruitment or medical procedures (such as laboratory technicians or data entry operators) in order to prevent interviewer or desirability bias. These staff members were trained in administering the comprehension test. They were also trained to note participants' spontaneous responses and not to guide the participants towards correct answers. After the comprehension test, participants were referred back to the study counsellors. After reviewing the scores and participants' answers, the aspects that were misunderstood or not understood were explained to the participants again by the counsellors. They were provided opportunity to ask their queries or questions again. Figure 1 illustrates the informed consent process used.

Consent comprehension questionnaire

Content

A structured consent comprehension questionnaire was used to assess comprehension of the informed consent form. It comprised questions on study objectives and procedures, risks and benefits, specimen storage, confidentiality and voluntary participation. There was also a question that ascertained participants' understanding that the information provided by the informed consent form was regarding the research that they were being requested to participate in. The questionnaire was pilot tested among 10 individuals reporting to the same clinic and with a similar education level and economic background. Both literate and illiterate participants were selected for pilot testing of the questionnaire. During pilot testing, it was assessed whether participants could understand the questions and the answering options clearly. The informed consent comprehension

questionnaire was finalised based on the results and inputs from the pilot testing for use during the informed consent process of the actual study. The test of understanding (questionnaire) had ten questions. Nine questions were asked to all of the enrolled participants, whereas the last question regarding disclosure of the HIV test result was applicable only to the HIV sero-positive participants among the HIV-discordant couples.

Scoring

The test of understanding was administered to all the study participants who were undergoing the enrolment informed consent process before asking them to sign the informed consent forms. Individuals scoring $\geq 80\%$ in the test were considered eligible for enrolment. This eligibility cut-off based on the score of test of understanding was determined on the basis of pilot-testing experiences and in consultation with the local ethics committee. Participants were enrolled after obtaining their signature in the case of literate participants or their left-hand thumb impression in the case of illiterate participants on the consent forms, with signatures of witness if applicable. Literacy was determined based on their ability to read and write the language of the consent form, i.e. 'Marathi' (the local language) or English. Participants were considered illiterate if they could not read and write 'Marathi' or English.

Statistical methods

Participants who were enrolled in the prospective cohort study after passing the informed consent comprehension test were considered for this analysis. Descriptive statistics were calculated for all enrolled participants ($n = 1337$) for their demographic and behavioural characteristics. Consent comprehension scores of the participants were converted into percent scores. Participants scoring $\geq 90\%$ in the test of understanding were categorised

Figure 1. Informed consent process [HPTN 034 Study]. NARI: National AIDS Research Institute (Pune, India).

into the 'optimal comprehension group', whilst participants scoring 80–89% were categorised into the 'lower comprehension group'. No-one scored <80%. Correlates of lower consent comprehension among the study participants were determined using univariate and multivariate logistic regression analyses. Data were analysed using SPSS v.15.0 (SPSS Inc., New York, NY, USA).

Results

Demographic and behavioural profile of study participants

A total of 1337 participants were enrolled in the cohort study. Data on consent comprehension were available for 1334 participants; 456 (34.2%) were men and 878 (65.8%) were women. The mean $\pm$ SD age of the men was 35.02 ± 6.96 years and that of the women was 28.99 ± 6.31 years. In total, 89 (19.5%) of the men and 466 (53.1%) of the women were ≤ 30 years of age. Less than one-quarter of the participants ($n = 283$) were illiterate, of whom 40 (14.1%) were men and 243 (85.9%) were

women. Monogamy was reported by 90/438 men (20.5%) and 766/873 women (87.7%). History of condom use ever was reported by 332/457 men (72.6%) and 423/877 women (48.2%). Moreover, 214/457 men (46.8%) and 866/878 women (98.6%) reported never consuming alcohol.

Comprehension of various components of the informed consent form

The mean $\pm$ SD percent comprehension score of informed consent was $94.4 \pm 5.00\%$ and was similar among men and women. Table 1 describes the comprehension of various sections of the informed consent form. The majority of participants (1323/1334; 99.2%) were aware that the informed consent form provided information regarding the research. Information pertaining to study-related risks was not optimally comprehended by 61.7% of participants, more so by men (306/455) than by women (517/878) ($p = 0.003$). Nearly 9% of the participants (117/1334) could not recall the tests/procedures that were supposed to be carried out during the study visits,

Table 1. Comprehension of various aspects of the informed consent form

Comprehension question (options given)	Answer	Men	Women	n (%) ^a
What does this consent form explain to you?	Don't know	1/11	10/11	11/1334 (0.8)
	Information about research study	455/1323	868/1323	1323/1334 (99.2)
Name any two difficulties you might face as a result of being in the study ^b	Wrong/partially correct	306/823	517/823	823/1333 (61.7)
	Correct	149/510	361/510	510/1333 (38.3)
After you sign this consent form, which tests/things will be done in this clinic? (Name any two things)	Wrong/partially correct	51/117	66/117	117/1334 (8.8)
	Correct	405/1217	812/1217	1217/1334 (91.2)
Which benefits would you get from this clinic as a result of being in this study? (Name any two things) ^b	Wrong/partially correct	11/63	52/63	63/1334 (4.7)
	Correct	445/1271	826/1271	1271/1334 (95.3)
Do you have to give your blood and other samples even if you do not wish to do so?	Don't know/yes	0/3	3/3	3/1334 (0.1)
	No	456/1331	875/1331	1331/1334 (99.9)
Will the information about you be given to the people not concerned with this study?	Don't know/yes	0/6	6/6	6/1334 (0.4)
	No	456/1328	872/1328	1328/1334 (99.6)
What will happen if you do not give your blood for testing?	You will not receive any treatment in this clinic	3/28	25/28	28/1333 (2.1)
	You will receive treatment and counselling in this clinic	452/1305	853/1305	1305/1333 (97.9)
If you participate in this study, do you have to come here for your study visits again and again?	No	0/1	1/1	1/1334 (0.1)
	Yes	456/1333	877/1333	1333/1334 (99.9)
What will be done with your leftover samples?	Will be thrown off immediately	1/12	11/12	12/1334 (0.9)
	Will be stored for future studies	455/1322	867/1322	1322/1334 (99.1)
Do you need to tell your HIV result to your spouse to be able to participate in the study?	Don't know/no	19/23	4/23	23/456 (5.0)
	Yes	373/433	60/433	433/456 (97.0)

^aData were missing for some participants for some of the questions.

^bStatistically significant difference between the two groups.

and 4.7% (63/1334) could not explain the benefits associated with study participation. In total, 11 (2.4%) of the 456 men and 52 (5.9%) of the 878 women ($p = 0.011$) did not understand the study benefits optimally. Comprehension related to other aspects of the study such as voluntary participation, confidentiality, similar access to standard care and study-related procedures (need for repeated visits, leftover sample, report disclosure to spouse) was high. Scores pertaining to these aspects ranged between 97% and 99% (Table 1).

Correlates of lower comprehension

Table 2 describes the correlates of lower consent comprehension and summarises the demographic and behavioural characteristics of participants in the lower comprehension and optimal comprehension groups.

In the univariate analysis, participants aged >30 years (OR = 0.71, 95% CI 0.55–0.93) and those reporting multiple partners (OR = 0.38, 95% CI 0.27–0.53) were less likely to have lower comprehension. Being an HIV-negative man (OR = 3.15, 95% CI 1.29–7.64) or HIV-negative woman (OR = 10.17, 95% CI 6.12–16.91), illiteracy (OR = 2.49, 95% CI 1.86–3.34) and lack of condom use (OR = 1.99, 95% CI 1.52–2.59) were more likely to be associated with lower comprehension. Interestingly, those who reported the habit of consuming alcohol were less likely to have lower comprehension. Employment status was not related to consent comprehension.

In the multivariate model, being an HIV-negative man (AOR = 4.36, 95% CI 1.71–11.05) or HIV-negative woman (AOR = 13.54, 95% CI 6.42–28.55), illiteracy (AOR = 1.65, 95% CI 1.19–2.30), history of multiple lifetime partners (AOR = 1.73, 95% CI 1.12–2.66) and lack of condom use (AOR = 1.35, 95% CI 1.01–1.82) were found to be independently associated with lower consent comprehension at a high level of statistical significance. Age, employment status and alcohol consumption were not associated with lower comprehension in the multivariate analysis.

As HIV-negative women and HIV-negative men were observed to have lower comprehension, a subset analysis was performed in order to explore the pattern for this association. Five categories, namely HIV-negative men and HIV-positive men (both from the discordant couples' cohort), HIV-negative women and HIV-positive women (both from the discordant couples' cohort) and HIV-negative women from the other women's cohort, were compared. The HIV-negative women from the other women's cohort were 13 times more likely to have lower comprehension (AOR = 13.76, 95% CI 4.18–45.28) followed by HIV-negative women from the discordant couples' cohort (AOR = 6.77, 95% CI 2.03–22.49) compared with HIV-positive men in the HIV-discordant couples' cohort (data not shown).

Discussion

The overall consent comprehension score of 94.4% indicates that the informed consent procedure resulted in a high level of comprehension of informed consent among the study participants. Comprehension about the study-related risks by the study participants was observed to be a challenge. Interestingly, whilst more women could comprehend study-related risks, more men could comprehend study-related benefits. Lower

comprehension scores were noted in the case of individuals who were HIV negative, illiterate, having multiple sexual partners and those who were not using condoms consistently.

The primary objective of the consent process is to ensure voluntary and non-coerced decision by the research participants to participate in research. Their decision should be based on adequate and accurate knowledge and understanding of the research. The high level of comprehension observed in this study could be attributed to initiation of the consent process through community education even at the pre-enrolment stage. Initiating the informed consent process at the community level has been stated to be one of the effective ways of enhancing the informed consent process based on the experiences from HIV Prevention Trial Network studies.²²

Comprehension of informed consent

Research participants should be able to understand the difference between clinical practice and participation in research, which may be an 'experiment'. Therapeutic misconception, i.e. inability of the participants to distinguish between the two, leading to inaccurately attributing therapeutic intent to research procedures,²³ can be a major challenge for the informed consent process for biomedical research.^{24,25} Studies in Thailand and India have reported that some participants failed to understand the real meaning of voluntariness,²⁶ and their willingness to participate resulted from the need for medical care associated with participation.¹⁵ Separating biomedical research facilities and healthcare facilities could be an important strategy to prevent 'therapeutic misconception'. However, the majority of participants from this study could understand that the informed consent form provided information about them being part of research and that they would not be discriminated from accessing standard treatment, even if they chose not to participate in the study. They could also understand that they have a right to choose whether or not they would give samples. Another study from India reported that maximum correct responses were obtained for the questions pertaining to participant's rights during consent comprehension assessment.¹³ High comprehension with respect to voluntariness in the current study might be attributed to the fact that two of the three study sites were located in research institutes and not in the hospital set-ups. In the case of the third site, although the location was on the hospital premises, the participants were recruited from the CIP of NARI that is oriented to recruitment in clinical trials. This might have prevented study participants from this study misinterpreting research as health care.

The observation that the study participants experienced challenges in comprehending information regarding study-related risks has also been made by other researchers.^{26,27} We feel that lower comprehension about 'risks' in the current study might be attributable to the nature of the study. This observational study did not involve the trial of any drug, device or intervention. The study offered no direct benefit and no more than minimal risks were involved. The risks explained in the consent form and during the consent process were discomfort during sample collection, embarrassment during physical examination or while providing the sexual history, and social hazards because of possible breach of confidentiality. The participants might not have perceived these as major 'risks' because they

Table 2. Correlates of lower consent comprehension among participants enrolled in a cohort study in Pune, India

Characteristic	LCG (n = 285) [n (%)] ^a	OCG (n = 1049) [n (%)] ^a	OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age (years)						
≤30	137 (48.1)	418 (39.9)	1		1	
>30	148 (51.9)	629 (60.1)	0.71 (0.55–0.93)	0.014	0.98 (0.74–1.33)	NS
Participant category						
HIV-positive men	17 (6.0)	375 (35.7)	1		1	
HIV-positive women	3 (1.1)	61 (5.8)	1.08 (0.30–3.81)	NS	1.31 (0.34–5.04)	NS
HIV-negative men	8 (2.8)	56 (5.3)	3.15 (1.29–7.64)	0.011	4.36 (1.71–11.05)	0.002
HIV-negative women	257 (90.2)	557 (53.1)	10.17 (6.12–16.91)	<0.001	13.54 (6.42–28.55)	<0.001
Education						
Literate	186 (65.3)	863 (82.4)	1		1	
Illiterate	99 (34.7)	184 (17.6)	2.49 (1.86–3.34)	<0.001	1.65 (1.19–2.30)	0.003
Lifetime partners						
Single	225 (80.6)	629 (61.1)	1		1	
Multiple	54 (19.4)	400 (38.9)	0.38 (0.27–0.53)	<0.001	1.73 (1.12–2.66)	0.012
Occupation						
Unemployed	81 (28.5)	255 (24.4)	1		1	
Employed	203 (71.5)	791 (75.6)	1.24 (0.92–1.66)	NS	1.08 (0.79–1.49)	NS
History of alcohol consumption						
Never	269 (94.7)	809 (77.4)	1		1	
Occasional	11 (3.9)	150 (14.4)	0.22 (0.12–0.41)	<0.001	0.83 (0.36–1.90)	NS
Frequent	4 (1.4)	86 (8.2)	0.14 (0.05–0.38)	<0.001	0.83 (0.25–2.73)	NS
Condom use						
Yes	123 (43.2)	629 (60.1)	1		1	
No	162 (56.8)	417 (39.9)	1.99 (1.52–2.59)	<0.001	1.35 (1.01–1.82)	0.043

LCG: lower comprehension group; NS: not significant; OCG: optimal comprehension group.

^aData were missing for some participants for some of the characteristics; therefore, numbers do not always add to the total in that group.

might have had experience of these discomforts sometime in their life. Adults have accumulated a foundation of life experiences and knowledge.²⁸ They connect any new learning to this knowledge or experience base. To help the participants comprehend study-related risks, study investigators should explore participants' experience and knowledge about the study procedures as well as their perceptions about the risk involved in such procedures.

More women demonstrated comprehension on 'study-related risks' than men. The majority of the female participants were HIV-negative women. They might have perceived quarterly HIV testing, physical examination and social risks to be undue hassles, as they would not usually get exposed to these procedures in routine life. This would have led to demonstration of better comprehension of study risks by women. Men had better comprehension of study benefits than women. The majority of men in the study were HIV-infected men. The study recruited participants in the pre-antiretroviral therapy roll-out period in India. The clinical care provided by the study to HIV-infected individuals was not easily accessible in other healthcare set-ups in India. This might have been reflected in better interest by HIV-infected individuals in learning study benefits and their better comprehension.

Determinants of lower consent comprehension

Targeting efforts on individuals with specific characteristics that are likely to affect comprehension of the informed consent as well as designing appropriate educational strategies might be possible to improve comprehension significantly. We explored the correlates of lower comprehension of informed consent in this study. Lack of education and knowledge of scientific concepts in biomedical research by potential participants is a known challenge for the informed consent process in developing countries.^{29,30} There are mixed reports regarding the association between education levels and levels of informed consent comprehension.^{24,31–34} Illiteracy was one of the barriers for optimal informed consent comprehension in the current study. In order to comprehend, a person must decode words and associate them with their meanings. Phrases and sentences must be dealt with fluently enough so that their meanings are not lost before the next ones are processed.³⁵ This process normally happens at a subconscious level at a rapid pace. When an individual is illiterate, he/she might require time to decode the language that he/she hears, in a manner comprehensible to him/her, and process the information before the next set of information is presented. In such cases, providing visual aids or anecdotal scenarios representing the research process that could

relate to real-life experiences might help the illiterate individuals in decoding the information and improving their comprehension. More studies are required to assess the efficacy of visual aids or anecdotal scenarios in improving comprehension of scientific concepts by illiterate individuals.

In this study, individuals having multiple sexual partners tended to have lower comprehension of informed consent. Similarly, HIV-negative individuals demonstrated lower comprehension. The concept of 'andragogy'²⁸ proposes that adults are relevancy-oriented. They must see a reason for learning something. In the current study, the HIV-negative participants, especially the HIV-negative women from the women's cohort who were unaware about the HIV status of their partners, demonstrated lower comprehension than HIV-positive men and women. The other category of HIV-negative women, i.e. women from the HIV-discordant couples' cohort, had better comprehension than the HIV-negative women from the other women's cohort. These women were aware about the HIV status of their partners and were participating in the study along with their partners. The risk perception as well as the felt need for care if detected to be HIV-infected might have been perceived to be more important by women from the HIV-discordant couples' cohort than women from the other category and this could have resulted in more interest in the study and greater comprehension.

Similarly, those with multiple sexual partners and not using condoms showed lower comprehension. These were the individuals who were at high risk of HIV acquisition and were probably unaware of their risk as demonstrated by their unsafe sexual behaviour. Because of their low health-seeking behaviour, they might not have perceived that the study would benefit them. They would have been reluctant in learning about the study, which might have affected their comprehension. Investigators must identify and explain the relevance that a particular study has to all categories of participants enrolled in the study and ensure a similar level of comprehension. This finding highlights that whenever a specific arm of participants is not receiving direct benefits from the study or if their problems are not directly addressed by being in the study, they need to be explained how their participation is important for the study endpoints in order to retain their interest in the study.

Limitations

The present study is a post-hoc analysis from the main study aiming at determining HIV incidence. During post-hoc analysis, the covariates were categorised into specific subcategories and were compared with the comprehension scores. The wide confidence intervals observed in the case of some study variables despite an adequate total sample size might be attributable to distribution of the study population among these subcategories of covariates which were not pre planned for this analysis. The study was not designed to develop a consent comprehension tool. As a result, the consent comprehension tool was not validated before its use. However, it was pilot tested for its finalisation for use in the study. Although we could observe the impact of sociodemographic factors on consent comprehension, we could not evaluate other factors such as interviewer bias, readability level of the consent form, psychological aspects as well as source of recruitment because this information was not

collected. In the main study, as the community education process was initiated before actual administration of informed consent, the study participants were relatively well informed. None of the participants was ineligible due to failure in achieving the desired level of comprehension. Hence, we could not explore areas of non-comprehension among intervention-naïve individuals. The study population had a certain degree of risk to HIV acquisition and may not represent the general population. Thus, the study findings have to be interpreted with caution as they may primarily apply to populations sharing specific characteristics. However, the findings of the study provide information about certain components of informed consent where there is a scope for improvement in comprehension.

Conclusions

Overall high comprehension scores observed in this study demonstrate that it is possible to achieve a high level of consent comprehension through a high-quality informed consent process in a developing country setting. Initiating the informed consent process at the pre-screening level in the community may enhance the quality of the informed consent process. Comprehension related to the study risks and procedural aspects still remains a challenge. Literacy levels, relevance of research to the potential participants, and their perceptions and attitudes may affect consent comprehension. A specially designed elaborate consent comprehension study in the general population would help to identify additional gaps in consent comprehension. These findings suggest that the study sites should take additional efforts among illiterate people, and those who do not have direct benefit from the study, to achieve adequate comprehension among them. A more intensive, interactive and client-centred consent process might help to enhance comprehension significantly.

Authors' contributions: SMM conceived the study and was the principal investigator; NSJ designed the study and designed the consent comprehension questionnaire (test of understanding); SSD and SS analysed the data; NSJ, SSD, SS, MVG, RCB and SMM interpreted the data; NSJ drafted the manuscript. All authors critically revised the manuscript for intellectual content and read and approved the final version. NSJ and SMM are guarantors of the paper.

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Ethical approval: This study was approved by the Institutional Scientific Advisory Committee, Ethics Committee, of the National AIDS Research Institute (Pune, India) and the Health Ministry Screening Committee of the Government of India. It was also reviewed and approved by the Institutional Review Board of Johns Hopkins University (Baltimore, MD, USA).

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