

Piloting a tool for informed consent comprehension in a cardiovascular clinical trial in South Africa: An IMPI-2 pilot trial substudy (ICC Study)

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Background. Informed consent is a key requirement in research. However, the comprehension of information presented is rarely evaluated prior to or during the research. Ensuring that participants understand the key issues in trials is important, not just for ethical reasons, but also because it can help set patient expectations. We evaluated the feasibility of using the University of California Brief Assessment of Capacity to Consent (UBACC) questionnaire to guide informed consent comprehension in the pilot study for the second Investigation of the Management of Pericarditis in Africa (IMPI-2) trial. IMPI-2 is a randomised control trial (RCT) on the use of alteplase-facilitated pericardial drainage, compared with routine care among patients with large pericardial effusion. We used an abbreviated version of the UBACC to evaluate participant comprehension of key elements of the consent documentation and to guide discussions.

Method. Comprehension was assessed using a 10-item UBACC at baseline, 6 weeks, 3 months and 6 months follow-up to reiterate the information about the trial. Each response was scored from 0 to 3 and the sum at each visit was recorded to represent comprehension. A UBACC score of ≥ 25 was considered adequate comprehension. Bivariate logistic regression was performed to evaluate comprehension over time. A multivariate analysis was conducted to identify predictors of UBACC score.

Results. The Informed Consent Comprehension (ICC) Study included 71 participants with a median age of 42 years; 45% were females and 49% had at least a secondary level of education.

Level of comprehension improved with time; the odds of passing the evaluation at baseline compared with 6 months was higher (odds ratio (OR) 1.39, 95% confidence interval (CI) 1.17 - 1.65, $p < 0.001$). Not using interpreters and having a secondary level of education were associated with higher comprehension. Despite knowing that they were participating in research, many participants still did not accept that the trial drug may have no effect.

Conclusion. It is feasible to use the UBACC questionnaire for informed consent comprehension evaluation in RCTs. Repeated learning during follow-up improves comprehension over time, while a low level of education and use of interpreters reduces comprehension.

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Informed consent is a voluntary agreement to be part of a research project by participants, following the presentation of sufficient information by the researcher or their delegates.^[1] It is a crucial component of research and requires availing the participant with accurate information on the purpose, risks and benefits of the study. It gives information about alternative methods of care available and ensures that participants understand how the information relates to their person and that their decision whether to participate or not is voluntary.^[2,3] However, the extent to which these requirements are achieved in research enrolment often remains a matter of researcher judgement in which empirical evaluation has no place.^[4]

Balancing completeness versus simplicity is a real challenge in the preparation of patient information materials. This need is more pressing in low- and middle-income countries (LMICs) because of the vulnerability of the population. Researchers, therefore, need to

ensure, in line with the Declaration of Helsinki, the comprehension of information they give to potential participants.^[5]

The process of informed consent is confronted by several challenges which include, but are not limited to: a conducive environment, presence of pain/distress,^[6] poverty, education,^[7,8] health literacy,^[9] presence of investigation intervention only in the context of the trial,^[10,11] insistence on signatures rather than oral agreement,^[12] use of voluminous and complex consent forms owing to the need to ensure legality,^[13,14] language barriers and foreign accents of researchers.^[9]

These challenges assume a larger dimension in resource-limited settings where populations have limited literacy. However, understanding of research concepts affects both developing and developed countries,^[15] and the focus should be on adapting the universal paradigms of research to local norms, ideas and literacy

levels. To obviate these challenges in obtaining consent, researchers must invent ways to make the process practicable and ensure that adequate information is provided to the participants to enable an unhindered and uncoerced decision. This may include changing from obtaining informed consent to providing all necessary supporting information and going the extra mile to ensure that potential participants clearly understand the study.^[16]

There has been considerable debate about the modalities of establishing comprehension in informed consent. Arguments on both divides have been on the veracity of basing participation in a trial on the comprehension of information provided to the participants.^[17-22] The need to establish this *prima facie* has led to studies on various approaches to test comprehension.

Some researchers have suggested an approach such as 'teach to goal',^[23-25] which can serve as an iterative tool to aid comprehension by emphasising a participatory consent process between participants and the researcher, rather than a one-off legalistic protocol.^[26] It is recommended that the researcher asks the potential participant short questions after the research has been described to assess that the potential research participant has at least a basic understanding of what the research involves. In a published report entitled 'Making health care safer' from the US Agency of Healthcare Research and Quality, the authors reviewed safety practices deserving widespread implementation. One of these practices was 'asking patients to recall and restate what they have been told during the informed consent process.'^[27] This is to ensure that patients have not only read and heard informed consent but, more importantly, understood the informed consent. Also, the National Quality Forum (NQF), an organisation chartered to develop and implement a US national strategy for healthcare quality measurement and reporting, released a report that endorsed healthcare practices aimed at improving patient safety throughout the healthcare system.^[28] One of these was that all healthcare professionals should ask patients to repeat or 'teach back' what they have been told by their provider during the informed consent discussion.

While using the combination of written and verbal explanation is time-consuming, the advantage of the 'teach back' method is that areas of poor comprehension can be identified, thus allowing further explanations to occur. Using the 'teach back' methodology can also identify patients who, despite repeated corrective feedback, have poor comprehension of the proposed research.^[24] It is doubtful if informed consent can be obtained from such patients. Reaching an optimum understanding of informed consent is best conceptualised as a process rather than a single event, extending beyond recruitment.^[29,30] The methods thus described help identify those that require a more thorough assessment of decision capacity and need remediation.^[31]

This understanding has led to the thinking that informed consent materials can be improved through an iterative learning process of firstly presenting the study information, secondly assessing a participant's understanding of the study elements, and finally revisiting and revising poorly understood elements.^[11]

Tools for consent comprehension

To address the need for comprehension of informed consent, different tools have been tried in different trials; among these are use of quizzes,^[32] structured questionnaires,^[33] brief informed consent evaluation protocol (BICEP),^[34] quality of informed consent test (QuIC),^[35] Deaconess Informed Consent Comprehension Test (DICCT)^[36] and the Digitised Informed Consent Comprehension Questionnaire (DICCQ).^[37] Each of these tools has presented their challenges, and is subject to different interpretations. In evaluating

comprehension, any tool used should enable the participant to understand the key elements of the trial and should ensure brevity and clarity while, at the same time, facilitate assessment of the decisional capacity of the participants. These attributes will aid the researcher in identifying participants who will need remediation.

One such tool that embodies these qualities is the University of California San Diego Brief Assessment of Capacity of Consent Questionnaire (UBACC), a simple 10-item screening tool.^[31] It was originally designed for use in evaluating capacity in participants being recruited into psychiatric research and could be a helpful tool in ensuring understanding of informed consent through repeated teaching and re-evaluation among research participants. The UBACC screens for participants' appreciation and understanding of research study elements including purpose, protocol procedure, risk-benefit and voluntary nature of participation.^[31] It has been used in schizophrenia,^[38] neurocognitive,^[39] HIV,^[40] and, recently, in genomics of schizophrenia research in South Africa (SA).^[41] In the genomics study, it was shown to be an effective tool for improving understanding of research elements. The UBACC has not been used in the African context in clinical trials and, in the current study, we decided to evaluate the feasibility of administering the UBACC among participants in the second Investigation of Management of Pericardial Disease in Africa (IMPI-2) pilot trial, a randomised control trial (RCT) of complete percutaneous pericardial drainage facilitated by intrapericardial alteplase compared with conventional pericardiocentesis when indicated in adults with large pericardial effusion due to tuberculous and non-tuberculous pericarditis.

IMPI-2 trial informed consent

Pericarditis is a prominent cause of heart disease morbidity and mortality in Africa, being responsible for 7 - 10% of heart failure admissions in the region.^[42] Pericardial effusion is a common sequel in most of the patients and this can lead to an emergency presentation in cardiac tamponade or, in a long-term complication, as constrictive pericarditis. These two complications are responsible for the mortality that results from pericarditis, with constrictive pericarditis having a mortality rate of 17 - 69% and a 6-month fatality rate of 26% in Africa and Asia.^[43]

The need to reduce the morbidity and mortality associated with pericardial disease led to the conceptualisation of the IMPI trial in Africa. The hypothesis of the IMPI-2 trial is that patients with large pericardial effusion randomised to intrapericardial alteplase to ensure complete pericardial drainage will have at least a 35% reduction in cardiac tamponade requiring pericardiocentesis or constrictive pericarditis, compared with conventional pericardiocentesis when indicated.

The pilot phase of the RCT is designed to study the feasibility of recruiting patients, retention and adherence to follow-up appointments to prepare the trial team for the commencement of a multicentre definitive trial.

We designed a substudy – the Informed Consent Comprehension Study (ICC Study) – in the pilot trial to evaluate the feasibility of using the UBACC as a training tool for iterative consent administration among participants to see if their comprehension of the IMPI-2 consent improves over time. The ICC Study also evaluated participants' acceptance of the 'teach to goal' method, as well as factors associated with better consent comprehension. To the best of our knowledge, this is the first time this kind of research has been done on clinical trials in Africa.

The hypothesis in the ICC Study is that use of the UBACC as a training tool will improve consent comprehension among participants of the IMPI-2 pilot trial. The main research question is: 'Does iterative

administration of UBACC as part of the consent process improve understanding of the trial protocol? Secondary questions to be addressed by the ICC Study include: (i) What is the baseline comprehension of consent information in the IMPI-2 pilot trial? (ii) Does comprehension improve with iterative learning? (iii) What do people remember over time? (iv) What aspects are consistently not understood? and (v) Is it purposeful to use the UBACC over time and, if so, what does it achieve? Our three major objectives in asking these questions are: to improve the understanding of consent in the IMPI-2 trial; to determine the influence of comprehension on adherence to follow-up over 12 months; and to evaluate factors that aid informed consent comprehension.

Methods

Data collection

Patients referred to the IMPI-2 pilot trial were screened for eligibility based on the protocol of the trial. This stipulates that the patient is aged ≥18 years, with no contraindication to fibrinolysis and with a confirmed presence of large pericardial effusion (echo-free space around the right ventricle of more than 1 cm at end-diastole). The following information was collected at baseline: a history of previous involvement in the trial, and demographic data such as age, sex, level of education, occupation and marital status.

Once eligibility was established, participants were taken through the consent process using a standardised consent form (available in English, Xhosa and Afrikaans) (Appendix 1). This included information on details of the study, currently available treatment, reasons for initiating the study, randomisation, risk and benefit, follow-up plan, duration of the study, confidentiality, voluntary participation and freedom to withdraw. An opportunity was given for questions and clarifications. We used a diagram of the heart with the two layers of the pericardial covering shown to illustrate the basic concept of pericardial effusion, pericardiocentesis and potential complications. A flow diagram was then used to explain randomisation and follow-up (Fig. 1). Those who did not understand English had interpreters to assist in the process.

Once the participant had no further questions, we administered the UBACC as a training tool in preferred language to evaluate participant comprehension (Appendix 2). The UBACC consists of 10 items presented as open-ended questions, with each item scored on a scale of 1 to

3, with 1 reflecting a clearly incapable response and 3 indicating a clearly capable response. An intermediate score of 2 may be used for partially appropriate responses or uncertainty even after re-explanation.

A total UBACC score following the first consent explanation was recorded. Items on which the participant scored 1 or 2 were then re-explained and a further opportunity for questions given, after which the UBACC was re-administered (Fig. 2). Where the UBACC was administered more than once, an average score was taken. In some situations, patients declined or deferred taking the UBACC evaluation after given consent to the IMPI-2 trial. In such instances, we then did the evaluation at the 2-weeks follow-up visit. For all participants, the average UBACC score at recruitment and at 2 weeks formed the baseline score.

At each follow-up visit (2 weeks, 6 weeks, 3 months and 6 months), we started by going through all information about the trial given in the consent process, but without formally re-consenting. This was then followed by an inquiry about new symptoms, drug use and general well-being. The patients were subsequently examined,

and echocardiography was conducted. Before concluding the follow-up visit, we assessed comprehension using the UBACC, and reiteration was done in areas where incorrect answers were given. At the end of the process, we conducted repeat evaluations and average UBACC scores recorded for the visit. This sequence of events was a side-effect of the fact that the ICC Study was introduced as a substudy only after the pilot trial had already been approved and started. At that time, the pilot trial team had already been trained and felt that the introduction of the UBACC was an imposition on their time. While in an ideal study the UBACC would have been administered before study data were collected, this was not possible for the ICC Study. Also, the UBACC was used as a training and monitoring tool, not as a screening tool. The ICC Study data collection was done from May 2017 to August 2018.

Sample size

To minimise the standard error of correlation of coefficient for reliability test, about 3 - 5 participants are recommended per question to provide a sample size that will

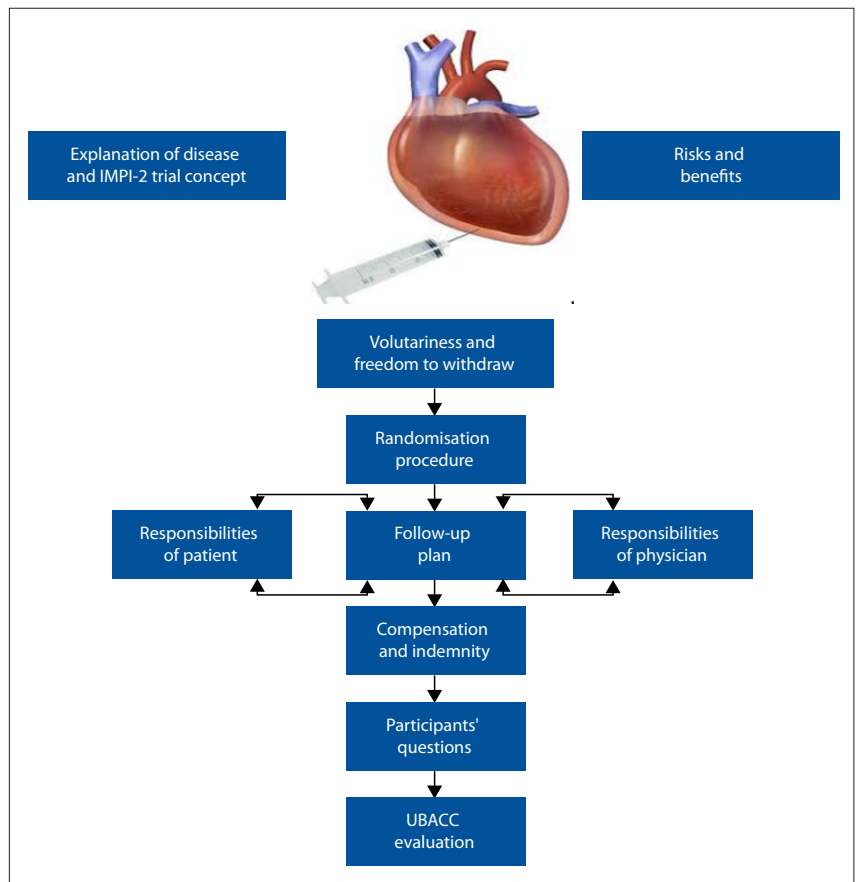


Fig. 1. Administration of IMPI-2 pilot trial ICC study evaluation protocol (IMPI = Investigation for Management of Pericarditis in Africa; UBACC = University of California San Diego Brief Assessment of Capacity to Consent; ICC = informed consent comprehension).

ensure the stability of variance-covariance matrix in factor analysis.^[44] The UBACC contains 10 questions, and based on the above recommendation, we calculated that a minimum of 40 participants (10×4) would be needed. Allowing for a non-response rate of 3 - 4%, a minimum for this was approximated to 55 participants.

Statistical analysis

Data management and analysis were done using STATA 14 (StataCorp, USA, 2013). Continuous variables were reported as mean with standard deviation (SD), while categorical variables were reported as count (%) and compared using the χ^2 test for categorical variables. Bivariate and adjusted logistics regression was performed for baseline and subsequent UBAAC scores to identify the relationship between factors such as age, sex, level of education, use of interpreters and different UBACC at baseline. Bivariate analysis was performed to determine the odds of passing UBACC at each follow-up visit compared against baseline, as well as the odds of passing the question after repeated explanation in subsequent follow-up visits. Multivariate logistics regression models were used to identify significant predictors of outcome at p -value < 0.05 ; odds ratio (OR) and 95% confidence interval (CI) were reported.

Ethical review

IMPI-2 trial participants' informed consent and patient information documentation were approved by the Faculty of Health Sciences Human Research Ethics Committee of the University Cape Town (HREC ref. no. 547/2016) and the South African Health Products Regulatory Authority (formerly Medicine Control Council of South Africa) (20150723). The trial was registered with clinical trials.gov (NCT02673879).

Results

Data included

From April 2017 to August 2018, a total of 300 participants were screened for eligibility into the IMPI-2 pilot trial. Out of these, 128 participants were recruited in the two centres (89 from Cape Town and 39 from Mthatha). This ICC Study was conducted at the Cape Town study site. Use of the UBACC tool for informed consent evaluation started in May 2017. The following were excluded from the analysis for various reasons: 7 participants had missed visits at 6 weeks; there were 2 deaths and 6 missed visits at 3 months; and 3 deaths and 5 missed visits were recorded at 6 months.

The first 8 participants did not have baseline UBACC data because the ICC Study approval was obtained 6 weeks after they had been recruited into the trial. The consent evaluation involved a total of 71 participants. The UBACC data available for analysis were as follows: 64 at baseline, 61 at 6 weeks, 50 at 3 months, and 35 at 6 months (Fig. 2). In total, we included 210 complete UBACC scores in our analysis.

Descriptive data

The demographic characteristics of the study population are displayed in Table 1. There was a slight male preponderance in the study (54.9%), most were within the age range of 30 - 49 years and the population median age was 42 years. Forty-nine percent had at least secondary level of education, 67.6% were of SA Xhosa origin and 33% needed interpreters for the interviews.

Baseline comprehension

The mean (SD) UBACC score at baseline was 23.8 (3.19); this increased with iterative learning at subsequent follow-up

visits compared with baseline as shown by significant improvement at 6 months (Fig. 1). The average score for Question 1 on the purpose of the ICC Study was lowest at baseline (Table 2).

Comprehension of different aspects over time

We recorded high UBACC scores in questions exploring the reason for agreeing to participate in the trial (question 2), voluntariness (question 4) and financial responsibility in cases of harm resulting from participation (question 10) (Table 3).

Knowledge of the primary purpose of participation in the trial (question 3) and right of withdrawal at any stage without effect on their continuing care (question 5) had a marked increase in UBACC scores at 6 months (Fig. 3).

Understanding of risk of participation (question 7), either resulting from the procedure, or as a side-effect of the trial intervention, remained poor. This was shown by the low UBACC score

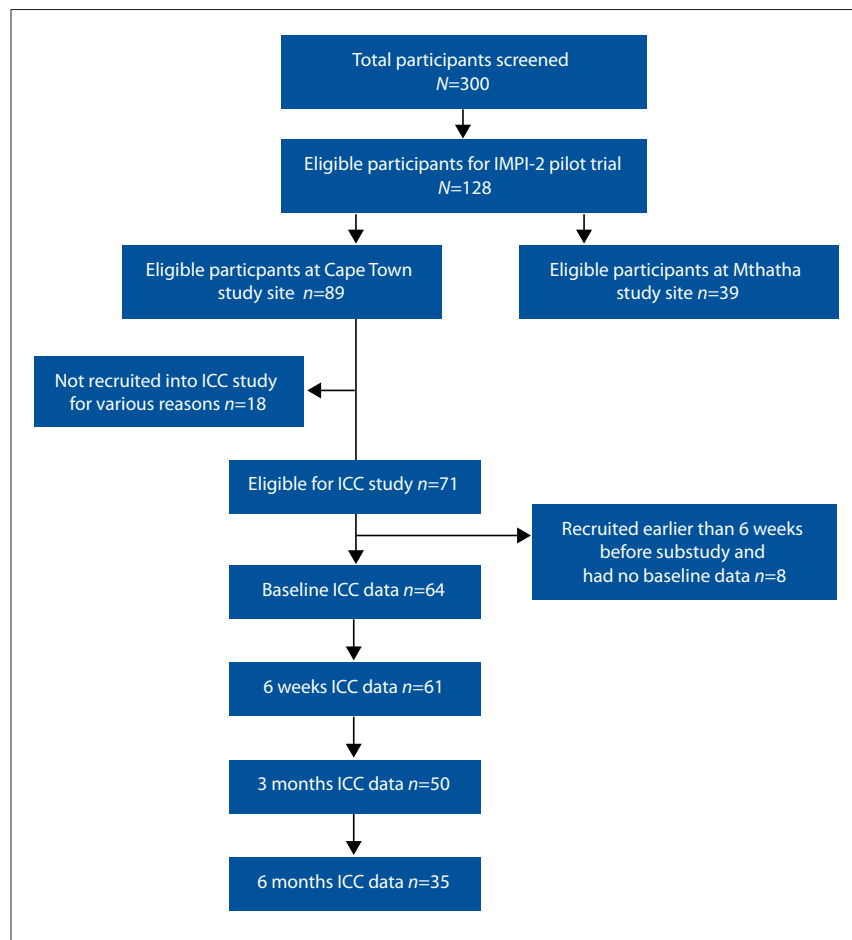


Fig. 2. The ICC Study flow chart (IMPI = Investigation for Management of Pericarditis in Africa; UBACC = University of California San Diego Brief Assessment of Capacity to Consent; ICC = informed consent comprehension)

throughout the study duration, which was worse at 6 months despite reiteration.

Comprehension of the uncertainty about the effect of the trial intervention (question 9) was low, but at 6 months there was a slight improvement.

Factors associated with higher UBACC score

Use of interpreters and having lower than a secondary level of education were associated with a low UBACC score, most marked at 6 months (Appendix 3). However, the study was hypothesis generating and not powered to test significance.

Understanding of specific questions

Most participants correctly answered UBACC question 10, ‘Who will pay for your medical care cost if you are injured as a direct result of

being in the study?’, with 78 - 90% correct response over the follow-up period. However, most participants failed to correctly answer UBACC question 9, ‘Is it possible that the treatment planned in study may not have the expected result?’, despite repeated correction (Fig. 4A).

Table 3 shows that, overall, participants’ comprehension improved with follow-up and this was most marked with regard to their understanding of the trial concept and the benefits, and that the primary focus was research. The question ‘Do you have to be in this study if you do not want to participate?’ was to establish the voluntariness of the IMPI-2 pilot trial. The understanding of this question was high throughout the follow-up.

Discussion

In this preliminary study, we showed that it was feasible to use the UBACC as a tool to track and improve informed consent comprehension among participants in an RCT, using the IMPI-2 pilot trial. Use of the UBACC as a training tool was acceptable to the IMPI-2 pilot trial participants. This provides further evidence to support the use of tools like the UBACC in clinical trial situations in LMICs, as previously suggested in a study in Africa among patients with schizophrenia.^[41]

At baseline, many participants did not understand the purpose of entering the trial. However, the level of comprehension measured by use of UBACC score improved with iterative learning over time. The level of comprehension also improved with repeated reinforcement over the follow-up period, which offers some evidence that reiteration improves comprehension, as seen in a study among HIV patients in Botswana.^[45] In this study, we used pictures and flow diagrams to explain different aspects of the trial, and emphasis was placed on the reiteration of areas where participants displayed low levels of comprehension. This could have accounted for the improvement we noticed over time.

Participants consistently understood the following about the trial: that the primary purpose of recruitment was research, that participation was voluntary, and that they were at liberty to withdraw with no consequences for their continued care. The majority were also aware that the researcher was liable in the event of harm. These are important aspects of research integrity, and improvement with reiteration as shown by improvement in UBACC score in the IMPI-2 pilot trial could strengthen adherence to follow-up.

Participants scored repeatedly low on questions relating to knowledge about the risk of the study, randomisation and on the certainty of the effect of the intervention. This was despite most of the participants knowing and acknowledging that the primary purpose of the recruitment was research (question 2). The finding may not be unrelated to the concept of therapeutic misconception and the complexities regarding explaining randomisation in LMICs, as has been alluded to by other studies.^[18,35] We can also attribute this apparent misconception to immediate relief from pericardiocentesis, leading some participants to see this as a proof of the good effect of the trial and ignoring the main trial intervention under investigation (use of intrapericardial alteplase). Some researchers have referred to this as a false expectation.^[46] The lack of comprehension among

Table 1. Baseline characteristics of the ICC study population

Characteristics	n (%) (N=71)
Age groups (years)	
<20	1 (1.4)
20-29	10 (14.3)
30-39	21 (30.0)
40-49	15 (21.4)
50-59	11 (17.7)
60-69	10 (14.3)
>70	2 (2.9)
Sex	
Female	32 (45.1)
Level of Education	
None	4 (5.6)
Primary [†]	21 (29.6)
Secondary	31 (43.7)
Tertiary	9 (12.7)
Population group	
South African blacks [‡]	48 (67.6)
Other South Africans [§]	13 (18.3)
Foreign nationals [¶]	10 (18.3)
Marital status	
Married	34 (47.9)
Single	35 (49.3)
Widowed	2 (2.8)
Previous trial	
Yes	68 (95.8)
No	3 (4.2)
Use of interpreters	
Yes	47(66.2)
No	24(33.8)

[†]Grouped with informal education.
[‡]Mostly Xhosa.
[§]White and Afrikaans.
[¶]Other African black immigrants.
 ICC = informed consent comprehension.

Table 2. Odds of passing UBACC at subsequent visits compared with baseline

Visit	n	Proportion passing (UBACC score >25), %	OR	95% CI	p (interaction)
Baseline	64	44.0	-	-	-
6 weeks	61	59.0	1.17	1.01 - 1.34	0.033
3 months	50	64.0	1.28	1.09 - 1.46	0.001
6 months	35	69.0	1.39	1.17 - 1.65	<001

UBACC = University of California Brief Assessment of Capacity to Consent; OR = odds ratio; CI = confidence interval.

Table 3. Proportion who passed the UBACC questions at baseline and follow-up

UBACC questions	Baseline, N=64				6 weeks, n=61				3 months, n=50				6 months, n=35			
	% pass	% pass	OR	95% CI	p-value	% pass	% pass	OR	95% CI	p-value	% pass	% pass	OR	95% CI	p-value	
Question 1 What is the purpose of the study that was just described to you?	36	51	1.15	0.99 - 1.33	0.061	60	60	1.27	1.08 - 1.48	0.003	51	51	1.20	1.01 - 1.43	0.044	
Question 2 What made you agree to participate in this study?	75	79	1.05	0.92 - 1.19	0.493	68	68	0.96	0.84 - 1.10	0.538	83	83	1.16	0.99 - 1.35	0.059	
Question 3 Do you believe that this is primarily research or treatment?	53	57	1.05	0.92 - 1.20	0.447	54	54	1.05	0.92 - 1.21	0.458	74	74	1.35	1.15 - 1.59	<.001	
Question 4 Do you have to be in this study if you do not want to participate?	78	85	1.07	0.96 - 1.20	0.219	84	84	1.06	0.94 - 1.20	0.303	80	80	1.05	0.92 - 1.20	0.475	
Question 5 If you withdraw from this study, will you still be able to receive regular treatment?	58	57	0.94	0.82 - 1.08	0.395	58	58	1.01	0.87 - 1.17	0.930	74	74	1.23	1.04 - 1.45	0.016	
Question 6 What are the things you are required to do while in this study?	66	59	0.94	0.80 - 1.10	0.426	54	54	0.88	0.74 - 1.04	0.131	60	60	0.94	0.78 - 1.14	0.533	
Question 7 Please mention some of the risk and discomfort that people in this study may experience	45	41	0.94	0.81 - 1.09	0.429	42	42	0.94	0.81 - 1.11	0.477	37	37	0.89	0.74 - 1.06	0.201	
Question 8 Please mention the benefits of being in this study	50	59	1.09	0.94 - 1.27	0.242	56	56	1.06	0.90 - 1.24	0.508	54	54	1.02	0.85 - 1.22	0.855	
Question 9 Is it possible that the treatment planned in study may not have the expected result?	42	39	0.97	0.83 - 1.15	0.732	38	38	0.96	0.82 - 1.14	0.663	60	60	1.19	0.99 - 1.44	0.069	
Question 10 Who will pay for the medical cost if you are injured as a direct result of being in the study?	78	84	1.05	0.93 - 1.19	0.400	90	90	1.13	0.99 - 1.28	0.077	80	80	1.01	0.87 - 1.18	0.850	

UBACC = University of California Brief Assessment of Capacity to Consent; OR = odds ratio; CI = confidence interval.

some participants could also mean that their primary concern was on the immediate relief following pericardiocentesis, rather than the long-term complication which the trial was designed to investigate. We tried to improve this with re-education and this could be the reason for the marginal increase in UBACC score on question 9 at 6 months. However, the preliminary IMPI-2 pilot data result shows that visit adherence at 6 weeks, 3 and 6 months was 78%, 80% and 75% respectively. This dropped further to 60% at 12 months

and the likely explanation for this trend, judging from the findings of the ICC Study, could be that non-adherence to follow-up is related to consent comprehension. Fig. 4A shows that at 6 months the proportion of participants with high UBACC score increased, despite the reduced number of participants. This could mean that those who had poor comprehension dropped out as a result of clinical improvement, while those who stayed on had better comprehension.

A higher level of education and non-use of

interpreters for UBACC administration were associated with a higher score, consistent with what has been reported previously in the literature.^[41,47,48] The low UBACC score for participants who took the evaluation in Xhosa could have been due to the difficulty in explaining such concepts as randomisation and research risk by the interpreters, who may not have the right words in the vernacular to convey the information to participants.^[9] Other explanations include the loss of meaning that could occur with the use of interpreters not adequately trained for the purpose and the influence of limited education on the understanding of concepts related to the study.^[49] This finding may also reinforce the opinion that use of investigators who have local language or accents different from those of research participants can affect informed consent comprehension.^[50,51] Reduced comprehension among those that used interpreters, compared with those that used the English language, could also imply the need for the development of culturally and linguistically appropriate tools for informed consent comprehension in communities, as advocated by some.^[37]

We attributed the low UBACC score seen with the low level of educational attainment to bias that could be shown by such participants to being tested. This is because they may have viewed the task of memory recall as didactic and embarrassing. This

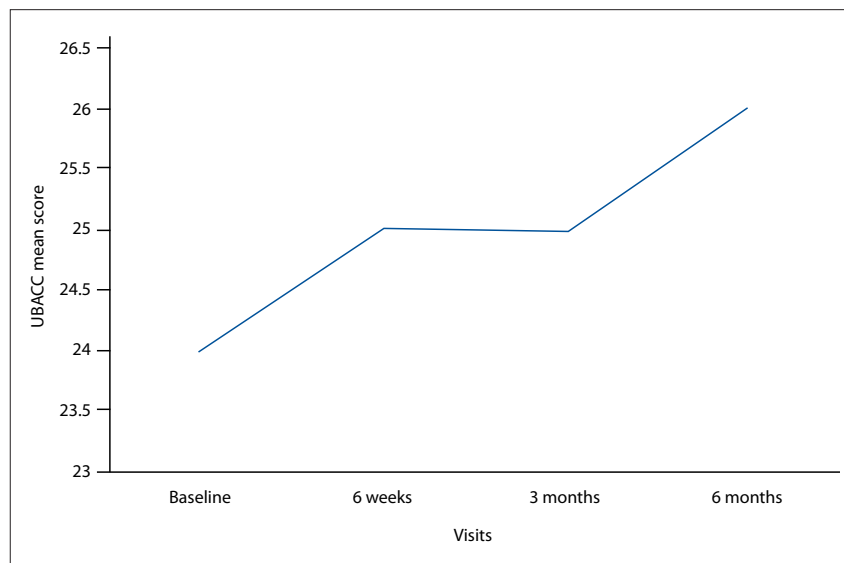


Fig. 3. Progression of consent comprehension with follow-up.

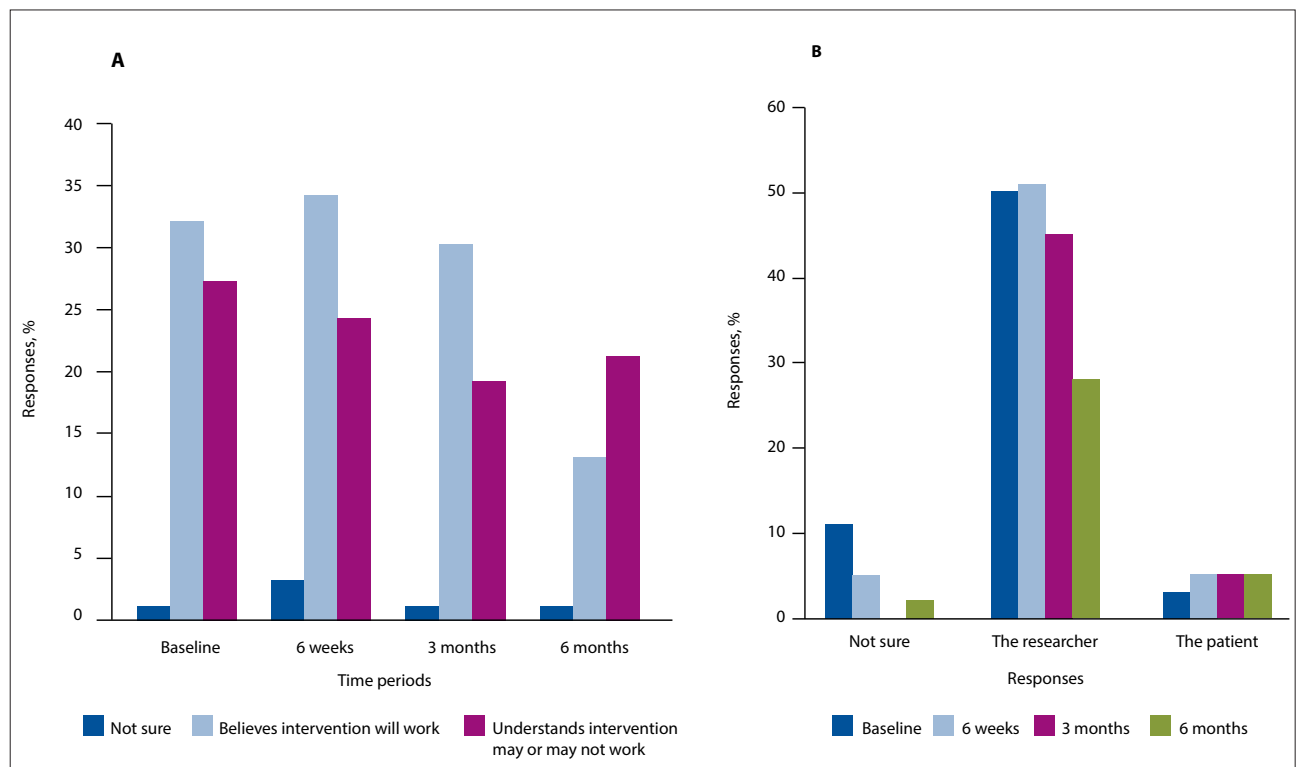


Fig. 4. Pattern of responses to (A) question 9 - 'Is it possible that the treatment planned in study may not have the expected result?' and (B) question 10 - 'Who will pay for your medical care cost if you are injured as a direct result of being in the study?'

has previously been shown to be a challenge to informed consent comprehension.^[26]

We noticed some secondary effects during this study, beyond the purpose for which it was primarily designed. The use of the UBACC to evaluate comprehension led to improvement in the skill and ability of the researcher in the administration of IMPI-2 trial informed consent to participants during the trial. With time the process became more structured and intuitive and led to prompt completion. This was beneficial especially in emergency situations, such as when patients presented in cardiac tamponade and time to intervention was crucial in achieving a good outcome. Also, the participants over time displayed knowledge of the trial concepts and took ownership of the process because of the iterative learning.

The study is limited by the small sample size and is not adequately powered to test association; this explains the large CI in the results. Therefore, our findings are mainly exploratory and will need to be confirmed in a larger main trial. The UBACC was conceived as a screening tool, but in this study, we used it as a teaching tool for improving comprehension of informed consent. Participants with low scores at baseline were not eliminated, whereas in the original concept low scores would have been understood as not having the capacity to consent. Another limitation of the study is having the researcher administer the evaluation which could have been a source of bias.

Conclusion

In conclusion, the use of an iterative learning tool such as the UBACC is feasible in an RCT and could lead to improved informed consent comprehension among participants. However, it may be better to use trained native language speakers to administer the consent process and evaluate comprehension. Effort should also be expended in the development of culturally and linguistically appropriate tools for informed consent comprehension based on local peculiarities.

Declaration. The contents of this manuscript are original and have neither been published or submitted for publication to any journal previously.

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Author contributions. GCI conceptualised this research, and wrote up the draft for submission. MAF conducted the statistical analysis in this research and was involved in writing up the statistical results. KS provided supervision throughout the research and read through the manuscript for intellectual content. LT was involved in initiation of the concept, provided guidance on the ethical/methodological rigor and read through every draft to ensure it was as planned. MN took over supervision of the research and read through the initial draft and subsequent edits for intellectual content to ensure we kept on track with the original concept. BM was the originator of the concept and provided excellent mentorship and insight into the research. JdV provided intellectual input on the research and provided expert guidance in arranging the research for publication.

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