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ABSTRACT

Background This pilot study evaluated the speaking book 'What it means to be part of a clinical trial'. The book aims at empowering populations with information on their rights and responsibilities when enrolled in clinical research. Wide publication of the book—at significant cost—is anticipated. It is important that the book is evaluated within the communities for whom it is intended, and the necessary changes (if any) are made, before translation and large-scale publication takes place.

Objective The objective of the study was to measure the efficacy and ease of use of the book.

Methods Participants were recruited from a catering company. Participants were questioned on their knowledge of clinical trials and were then given the book. Instructions for use of the book were given to one group ('experimental' group). The other group ('control' group) was not given any instructions. A week later, the investigators returned, repeated the knowledge questions and asked 'ease of use' questions.

Results A two-way repeated measure of covariants showed a statistically significant positive increase in knowledge of clinical trials among the intervention group ($p=0.02$). Results for the control group displayed trends that were not statistically significant. Percentage analysis of 'ease of use' questions proved that the book is easy to use, although some changes would be beneficial.

Conclusion This study revealed that the speaking book is easy to use. It significantly increased knowledge of clinical trials among the study sample if instructions on use of the book were provided.

'What it means to be part of a clinical trial' is a battery-operated 'speaking book' targeted towards developing world communities with a low literacy level who are likely to have access to clinical trials, either by volunteering themselves, or because a family member or friend is a clinical trial participant.

The speaking book explains in simple English what it means to be part of a clinical trial. Speaking books have hard covers and large pages. Each page of the book is vividly illustrated, with simple text pertaining to the illustration. Every speaking book has a plastic panel running down the right-hand side enclosed in which is a battery. The panel hosts a series of push buttons, each of which corresponds to a specific page in the speaking book. When activated, the 'push buttons' trigger a soundtrack of the text on the relevant page. The soundtrack, which is narrated by somebody with the appropriate voice and tonal quality, is thus 'read' to the person using the book. This makes the speaking book ideal for those who live in developing countries where literacy levels are low.

The speaking book has potential as an instrument for worldwide use if it is adapted for a relevant language and culture. Our pilot study aimed to evaluate the ease of use and extent of knowledge gain arising from usage of the speaking book over the period of a week. The study was also intended to expose problems with the book that could be practically addressed before translation and wider publication.

WHY DO WE NEED THIS SPEAKING BOOK IN THE DEVELOPING WORLD?

Knowledge of clinical trials in the developing world

Over the past few decades, the number of international clinical research projects taking place in the developing world has increased significantly. Among the reasons for this is the fact that research costs are lower in these countries, and it is much easier to find participants who have never received treatment for their condition, so-called drug-naive patients.[1]

Research ethics committees in developing countries emphasise the fact that research populations in these countries are vulnerable to many forms of exploitation resulting from unethical research. The causes of this vulnerability include low literacy levels, poverty and socioeconomic structures. Some research participants are vulnerable not only by virtue of residing in a developing country, but also because of adverse social and political influences within the country, which may make potential research participants subordinate to others.[2]

It has been suggested that in developing world settings, empowerment should constitute an ethical requirement in research involving vulnerable, oppressed and non-majority groups.[3] Empowerment, it is argued, will help to close channels by which research participants are sometimes open to exploitation. The speaking book aims to empower vulnerable populations.

How bad is the situation?

There are many aspects of clinical trials that those living in developing countries do not understand. Work done in Kilifi, Kenya, suggests that misunderstandings have contributed to concerns and rumours, which potentially undermine ethical aspects of research and local trust in the institution.[2] Other studies showed that participants

believed medicines had already been tested for safety and efficacy; that they would be assigned to a study arm based on their health needs, and that the trial was designed to benefit them (thus perpetuating the therapeutic misconception).[4]

Not only do potential participants need knowledge of what it entails to be part of a clinical trial, but they also need to be empowered on issues around justice. They need to understand that researchers and sponsors have an ethical obligation to ensure post-trial access to the confirmed intervention—at the very minimum this should be afforded to all the research participants. Any other benefits of the clinical trial also need to be shared.[5] Potential clinical trial participants need the assurance that they do not have to bear the costs of trial-related injuries or harms sustained as a result of participation. When a sponsor embarks on a clinical trial careful consideration needs to be given to the competing interests of optimising scientific progress and simultaneously protecting the rights and dignities of the participants in the research process. Furthermore, when these trials are conducted in the developing world, the tenets of distributive justice need to be emphasised.

Researchers have a responsibility to ensure that patients' participation is informed and voluntary.[5] This responsibility implies that we should strive continuously to improve the effectiveness of methods for informing prospective research volunteers about experimental studies, thereby enhancing the protection of their interests.

Some recommendations to address this challenge are as follows:

- Ask prominent and well-respected community-based figureheads to identify barriers to adequate informed consent in their community.[6]
- Disseminate information through numerous different channels.[1]
- Use varying types of consent form.[3]
- Make use of drama scripts, songs, partner letters, fact sheets and similar project information materials.[7]
- Maintain a list of frequently asked questions regarding clinical research.[6]

Rationale behind the speaking book

It is important that any intervention designed to raise awareness of clinical trials is targeted to the literacy level of the potential study population.[8] In order to address this concern, the speaking book is very simple, with multimedia functionality that allows for the enhancement of understanding.

Some express concerns about achieving a balance between effective information dissemination and information overload: 'Certainly, the (informative) process must convey to participants the host of responsibilities and behaviours that will be expected of them during the research period, but researchers have found it challenging not to exceed an individual's absorptive capacity on any given occasion.'[6] Information overload is not a concern when it comes to the speaking book. This is because the book can be taken home, shared with family members or friends, and there is no pressure to absorb all the necessary information in a condensed time period.

METHODS: A DESCRIPTIVE, CROSS-SECTIONAL, QUESTIONNAIRE-BASED STUDY

The study was approved by the Human Research Ethics Committee (Medical) at the University of the Witwatersrand (protocol number M090121). Permission to conduct the study among its staff was also obtained from a company providing mass-catering services. The study population comprised university-based catering staff.

Having obtained their informed consent, participants from two different geographical locations of the university were recruited into two separate groups in order to avoid contamination of data.

Inclusion and exclusion criteria for the study were: Equal numbers of men and women (15 men and 15 women) in each study group. A minimum participant age of 18 years and a maximum age of 50 years. Minimal literacy levels demonstrated by participants. Participants were thus able to understand spoken English but had difficulty reading it, or could not read it at all. The investigators evaluated reading skills among the participants by asking them to read from a page in the speaking book. This evaluation of reading ability was subjective and thus may be seen as a limitation of this study. Individuals who had taken part in a clinical trial previously were excluded from the research.

Following enrolment, the predistribution questionnaire was administered. This questionnaire was used to gauge baseline knowledge of clinical trials in the study population before distribution of the speaking book. Upon completing the predistribution questionnaire, every participant was given a speaking book. The participants in the intervention group were given verbal instructions on how to use the book, as well as a demonstration. The participants in the control group were not given any instructions. A follow-up meeting in a week's time was then scheduled with each participant.

At the follow-up meeting the post-distribution questionnaire was administered. The first section of this questionnaire was a repeat of questions from the predistribution questionnaire in order to gauge the extent to which knowledge of clinical trials had been enhanced (if at all) by the speaking book. The second section was designed to evaluate ease of use of the speaking book.

RESULTS

Results were measured in two different ways. Those pertaining to the knowledge of clinical trials were subject to a two-way repeated measure analysis of covariants using SAS version 9.1. This allowed us to establish whether there had been a change in the knowledge of clinical trials. Those pertaining to ease of use of the book were subject to percentage analysis.

Knowledge

Before the two-way repeated measure was calculated, responses were numerically converted. 'Yes' was converted into 1 and 'no' was converted into 0. A mean (average) score for the 11 questions was then computed on an individual basis. The baseline mean score was computed at time 1 (t=1) and the post mean score was computed after the week at time 2 (t=2). This reduced the data into three sets: (1) individual scores; (2) group scores (control and experiment); and (3) two measures (baseline mean and post mean).

A repeated measures analysis of variance method was then used to identify if there were any significant differences between the two groups and between the repeated measures (baseline mean and post mean). Interactions between the two groups (SAS for Windows version 9.1) and repeated measures (times) were also identified.

The two-way repeated measure analysis produced some interesting results. The main effect for group was not found significant: $F(1,51)=1.53$, $p=0.22$. The main effect for time was also found not to be significant: $F(1,51)=0.16$, $p=0.7$. However,

the group*time interaction was found to be significant: $F(1,51)=8.21$, $p=0.01$. Tests for simple effects showed that the mean scores for the control group displayed no significant difference across time: $F(1,26)=0.76$, $p=0.39$. However, the intervention group displayed a significant increase in score across time: $F(1,26)=6.11$, $p=0.02$.

One possible reason for this divergence of results pertaining to knowledge is that the baseline could have been obtained mainly through guess-work as few participants had heard of clinical trials. In the control group, it became evident that many of them did not know how to use the book—even after having it for a week. This could mean that the control group, for the most part, continued guessing the answers when the post-distribution questionnaire was administered. This theory about guess-work is backed up by the fact that the decrease in knowledge of the control group is not statistically significant.

Analysis of questions

Question 1

At the initial interview, participants were asked if they had heard of clinical research. Twenty-seven participants from the intervention group and 18 participants from the control group had not (this constituted 62.5% of the entire sample). After usage of the book, most participants (C_n Y=26, I_n Y=26; 96.3% of total sample) responded that they had now heard of clinical research. Whereas the numbers increased in the control group (C_n Y=10 to C_n Y=26) an analysis of the subsequent questions reveals little understanding of trial participation. This problem was not encountered in the intervention group (table 1).

Question 2

When asked what happens in a clinical trial, 19 participants from the control group and 14 from the intervention group answered that medicines are tested (68.7% of the total sample). At the follow-up interview 94% of the total sample answered this question in the affirmative (C_n Y=25, I_n Y=26). These results suggest a substantial increase in understanding of clinical trials.

Question 3

When participants were asked whether they could withdraw from clinical trials, 10 participants from the control group and 18 from the intervention group stated that withdrawal was not permitted (58.3% of the total sample). Following use of the book, there was a dramatic improvement in both groups: 75.9% of the entire sample (C_n Y=20, I_n Y=21) understood that one is allowed to withdraw from clinical trials at any time.

Question 4

'If a clinical trial is being conducted at a hospital or clinic which you attend, will you have to participate?' Before use of the book, 22 participants in the control group and 26 participants in the intervention group answered 'yes' to this question. During follow-up interviews, it was noted that 13 participants from the intervention group still answered this question in the affirmative. This result suggests that text, and its positioning in the book, may not carry enough emphasis with regard to voluntary participation.

Question 5

Asked whether all medicines given to them in a clinical trial would make them feel better, 74% of the total sample (C_n Y=23 and I_n Y=14) said that this was the case. At the follow-up interview 54% still responded in the affirmative to this question (C_n Y=12, I_nY=16). Page 4 of the speaking book, which pertains to this question, reads as follows:

> 'Taking part in a clinical study means you may get the chance to get treated with new medicines that aren't in chemists yet. The information received from the study may help treat people with your illness in a better way. Your illness may also improve but if the

Table 1 Responses to knowledge questions

	Control				Intervention			
	Initial		Follow-up		Initial		Follow-up	
No Question	No	%	No	%	No	%	No	%
1. Have you heard of clinical research?	Y=10	36	Y=26	96	Y=1	3.5	Y=26	96
	N=18	64	N=1	4	N=27	96.5	N=1	4
2. Are medicines tested in clinical trials?	Y=19	76	Y=25	92.6	Y=14	56	Y=26	96
	N=4	24	N=2	7.4	N=11	44	N=1	4
3. Once you start a clinical trial, can you stop whenever you like?	Y=12	54	Y=20	74	Y=8	30	Y=21	78
	N=10	46	N=7	26	N=18	70	N=6	22
4. If a clinical trial is being conducted at a clinic or hospital that you attend, will you have to participate?	Y=22	85	Y=5	19	Y=26	93	Y=13	48
	N=4	15	N=22	81	N=2	7	N=14	52
5. All medicines given to you in a clinical trial will make you feel better?	Y=23	88	Y=12	44	Y=14	58	Y=16	64
	N=3	12	N=15	56	N=10	42	N=9	36
6. Do you have any rights when taking part in a clinical trial?	Y=24	92	Y=27	100	Y=26	96	Y=25	93
	N=2	8	N=0	0	N=1	4	N=2	7
7. Are you allowed to ask questions about the trial?	Y=24	89	Y=26	96	Y=25	89	Y=27	100
	N=3	11	N=1	4	N=3	11	N=0	0
8. Are you allowed to discuss the trial with your family?	Y=25	93	Y=26	96	Y=24	86	Y=25	93
	N=2	7	N=1	4	N=4	14	N=2	7
9. Do you need detailed information about your participation?	Y=26	96	Y=27	100	Y=25	93	Y=26	96
	N=1	4	N=0	0	N=2	7	N=1	4
10. Will your information from the clinical trial be shared with other people?	Y=22	88	Y=3	11	Y=19	70	Y=5	19
	N=3	12	N=24	89	N=8	30	N=22	81
11. Will participating in a clinical trial earn you extra money?	Y=10	45	Y=3	12	Y=12	46	Y=5	10
	N=12	55	N=23	88	N=14	54	N=20	90

trial medication is not effective or you receive a placebo, which is a sugar pill, you may not benefit from taking the study medicine, but you will learn how to cope with your illness.'

It is possible that sentence one (above) is open to misinterpretation and suggests that one will be getting 'treatment', which is not the case in clinical trials. The final sentence might also be misleading.

Questions 6–9

'Do you have any rights when taking part in a clinical trial?'; 'Are you allowed to ask questions about the trial?'; 'Are you allowed to discuss the trial with your family?' and 'Do you need detailed information about your participation?' During the first interview with participants, the majority in both the control and the intervention group answered 'yes' to questions 6, 7, 8 and 9 (Q6: C_n Y=24, I_n Y=26; Q7: C_n Y=24, I_n Y=25; Q8: C_n Y=25, I_n Y=24; Q9: C_n Y=26, I_n Y=25). Although the participants did not know about clinical trials, most were aware that they have certain rights that can be generalised to all situations. This suggests that the notion of a 'rights-based society' is becoming more prominent in the South African context. Furthermore, the participants had some exposure to university students, and perhaps this could have been influential.

Question 10

'Will your information from the trial be shared with other people?' During the first questionnaire session with participants, 22 members of the control group and 19 members of the experimental group answered 'yes' to this question. This reveals that there may be little knowledge about the concept of confidentiality among the target population. There was a definite improvement in this knowledge at the follow-up sessions (after exposure to the speaking book) with only three members of the control group and five members of the intervention group answering 'yes' to this question.

Question 11

At the end of the research almost all the participants were aware of the fact that clinical trials are not a means to earning money. 'Will participating in a clinical trial earn you extra money?' (C_n N=23, I_n N=20). These results suggest that the speaking book addresses information on undue inducement somewhat effectively. This is important in a country such as South Africa where poverty is rife and communities are vulnerable to exploitation.

Ease of use

Ease of use of the book was calculated by computing 'yes' and 'no' answers to the 'ease of use' questions and then calculating a percentage. A limitation of the 'ease of use' section is its subjectivity in the sense that it was based on opinions of the book. On the whole, there is an overall consensus that the book is easy to use, helpful and informative. It is important to note the fluctuations in group number for the 'ease of use' questions. This is due to some participants who were unwilling to answer certain questions, or who did not know the answer to certain questions. Only definite 'yes' and 'no' answers were recorded.

Control group versus experimental group

Initially, when we asked the control group of 27 whether they found the book easy to use, 100% said 'yes'. However, one person did not try to read the book and another said there had not been enough time to do so. Further questioning revealed that in actual fact, only 56% of the control group had worked out that the push buttons on the panel corresponded to specific pages in the book. This suggests that although it was easy to push the buttons and listen to the narration, the overall concept of the 'speaking book' actually 'reading' the pages to you was missed in the control group (table 2).

Results from the experimental arm of 27 participants showed that 89% of participants found the book easy to use. Furthermore, 81% of the participants knew that the pushbuttons on the panel corresponded to the pages of the book. This is consistent

Table 2 Responses to questions on 'ease of use' of the speaking book

	Control				Intervention			
	Yes		No		Yes		No	
No Question	n	%	n	%	n	%	n	%
1. Did you find the book easy to use?	25	100	0	0	24	89	3	11
2. Do you know that each page in the book corresponds to a certain push button?	15	56	12	44	21	81	5	19
3. Did you find the book helpful?	23	92	2	8	26	96	1	4
4. Did you understand the words in the book?	24	89	3	11	21	81	5	19
5. Did you like the pictures?	25	100	0	0	27	100	0	0
6. Did you show the book to other people?	21	78	6	22	23	85	4	15
7. Did you discuss the book with those to whom you showed it?	16	76	5	24	18	78	5	22
8. Did these others who looked at the book think it was informative?	18	95	1	5	22	100	0	0
9. Do you want any changes to the book?	6	23	20	77	5	19	21	81
10. Do you know what makes the book work?	24	89	3	11	27	100	0	0
11. Do you know where the on/off switch is?	26	96	1	4	27	100	0	0
12. Can you explain how the battery is changed?	14	52	13	48	16	59	11	41
13. Would you be able to change the battery? (Do you have a screwdriver with which to do so?)	15	56	12	44	10	37	17	63

with the fact that the use of the book was explained to the intervention group.

Ninety-two per cent of the control group said they found the book helpful, although this was not evidenced in the mean score for this group, which revealed little change in knowledge. Ninety-six per cent of the intervention group found the book helpful.

Eighty-nine per cent of the control group said they understood the words in the book. When asked which words they did not understand, the 11% who had expressed concern could not remember which words they struggled with. Eighty-one per cent of the intervention group said the words in the book were easy to understand. Of the 19% who had difficulty, many said that hearing the words repeated over and over aided understanding, as did the pictures. All (100%) of the participants in the study said they liked the pictures in the book.

Two-thirds of the control group showed the book to other people; there was a certain amount of discussion with them and, for the most part, others who saw the book found it informative. Eighty-five per cent of the intervention group showed the book to other people. The majority of participants discussed the book with families, friends and neighbours. All other parties found the book informative in the experimental group.

Twenty-three per cent of the control group said that certain changes should be made to the book. Nineteen per cent of the intervention group thought that changes should be made to the book. The main suggestions were to add more information and make it easier to change the battery.

In the control group, 11% did not know that the panel on the right of the book held the apparatus for the operation of the book compared with the experimental group in which all participants were aware of this. One participant in the control group had not managed to locate the 'on—off switch', whereas all in the experimental group knew where it was. Fifty-two per cent of the control group had worked out how the battery was changed, but 44% of the group stated that they did not own the screwdriver necessary to change the battery. Fifty-nine per cent of the intervention group knew how to change the battery, but only 37% said they had a screwdriver with which to do so.

DISCUSSION

Results reveal that the speaking book is highly efficacious when its use is explained to those who receive it. While it is important to instruct participants on the use of the book, it is evident from the breakdown of individual questions that even those who do not receive instruction can benefit from the book. On average, the participants in the intervention group also found the book much easier to use.

We recommend that speaking books do work and should be widely distributed, especially in regions where clinical trials are frequently conducted. However, instructions on the use of the book should be a prerequisite to distribution. In a primary healthcare clinic setting giving verbal instructions might be a possibility. Another possibility is that the book is distributed by research units who can take time to give explanations. Explanations on a group basis might be sufficient, as the group could teach each other how to use the book. Logistics such as changing of batteries could be arranged with clinics and research units. Recipients of the books should be advised that they may approach clinics for this.

Our research demonstrated that, in general, the research participants (from the target population) understood the text in the book. However, there were a few exceptions, as noted in the results section, which we will address.

Speaking books have been developed on various topics including tuberculosis, HIV and depression.[9] We also recommend that institutions that distribute speaking books in practitioner waiting rooms, rural facilities and other venues arrange that someone is on hand to explain how the book works to those who wish to read it. Our research has clearly shown that this is necessary, and it would be a pity if other speaking books that have promising educational value were not having maximum impact.

Researchers conducting clinical trials are encouraged to use the speaking book as a starting point. The speaking book could be used as a tool to complement the informed consent process.

CONCLUSION

This study evaluated the speaking book 'What it means to be part of a clinical trial' in an environment that appropriately represented the demographics of the populations to whom it is targeted. We aimed to expose areas in which the speaking book could be improved as well as determine the strengths of the speaking book before translation into the appropriate vernacular, mass printing and publication.

It is hoped that through initiatives like the speaking book, people in the developing world will have the opportunity to empower themselves before enrolling into clinical trials. Such interventions will contribute towards balancing out asymmetric power relationships, which are all too prevalent in research involving humans.

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Competing interests One teaching post at the Steve Biko Centre for Bioethics (the occupant of this past was not involved in this research) and some activities of the Centre have been sponsored by Pfizer.

Ethics approval This study was conducted with the approval of the University of the Witwatersrand, Johannesburg, Human Research Ethics Committee (Medical).

Patient consent Obtained.

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