

Does an HIV clinical trial information booklet improve patient knowledge and understanding of HIV clinical trials?

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Objectives

To evaluate the impact of an information booklet on HIV clinical trials, *Clinical Trials in HIV and AIDS: Information For People Who Are Thinking About Joining a Trial*, in addition to the standard trial information (SI) on patients' knowledge; understanding and attitudes about clinical trials; and to investigate patients' motivations and reasons for enrolling or not enrolling in a clinical trial.

Methods

Fifty HIV-1 positive patients who attended the HIV clinic at a west London hospital were randomized to receive either SI alone ($n = 27$) or SI and a 16 page information booklet explaining the principles and procedures of HIV clinical trials ($n = 23$). A self-administered questionnaire was used at baseline to assess past experience and attitudes to clinical trials (10 questions), knowledge and understanding of HIV treatments (8 questions) and clinical trials (11 questions). At 2–6 months after randomization, a second interviewer-administered questionnaire addressed the patient's assessment of the usefulness and comprehensiveness of the information provided by the SI and information booklet, whether or not the patient had enrolled in a clinical trial and reasons for enrolling/not enrolling, knowledge of specific aspects of the trial protocol the patient was eligible to join (13 questions) and general knowledge of clinical trial procedures (repeat of 11 baseline questions). Changes in the attitudes and scores on knowledge and understanding of clinical trials were compared for the two groups.

Results

In both groups, patient knowledge of clinical trial procedures improved significantly over the study period. The median score increased from 30 at baseline to 35/44 at follow-up (SI only) vs. 24–31/44 (SI plus booklet), but this did not differ significantly between the two groups. However, knowledge of the specific trial protocol was poor [median score 13/25, interquartile range (IQR) 8–14], and there was no difference in the scores for the two groups. The prime motivations for joining a clinical trial were to benefit personal health and to gain access to new treatments. Potential side-effects were the main concern of prospective trial participants.

Conclusions

This small trial shows that, while the patients' general knowledge and understanding of clinical trials improved over time, this was not improved by the information booklet and recollection of the details of the relevant trial protocol remained poor.

Keywords: clinical trial, HIV, understanding, knowledge

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Introduction

Adequate and timely recruitment of patients remains a substantial problem for many clinical trials [1,2], and only a small proportion of potentially eligible patients actually enrol in a clinical trial [3,4]. Impediments to enrolment

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include restrictive eligibility requirements [5–7], and a reluctance of physicians to refer patients for trials [3,5,7–9]. Since patients frequently do not have ready independent access to information about ongoing clinical trials, their awareness of a particular trial is dependent on the physician initiating a discussion about the study [8–10]. However, even when patients are offered the option of enrolling in a trial, studies suggest that between 30 and 40% of eligible patients elect not to take part [3,4,6]. The main reasons given by patients for not enrolling in a clinical trial are concerns about side effects of the particular study drug(s), that they are too unwell, fear of being a ‘guinea pig’ and time constraints [4,6,10–12].

A further concern is that, even with conventional informed consent, patients often misunderstand or forget basic practical information relating to the trials they are participating in [13–17]. There is therefore a need to provide patients with clearer information about clinical trials to enable them to make more informed decisions. However, it remains unclear exactly what information patients consider helpful in their decision to join a trial, and whether different educational strategies may work better in different groups of patients. Various methods of improving patient knowledge and understanding of clinical trials during the informed consent process have been evaluated, such as discussion groups, booklets and videotapes [18–22].

In 1991, a general patient information booklet about clinical trials was developed [23]. An evaluation of this among 58 health professionals and 39 patients suggested the need for more disease-specific information [24]. Therefore, in 1993 an HIV specific patient booklet was devised entitled, *Clinical Trials in HIV and AIDS: Information For People Who Are Thinking About Joining a Trial* [25]. This was intended for use by patients and also by doctors and nurses counselling patients about trials, to supplement the more detailed information provided about a particular study protocol.

We conducted a randomized trial to evaluate the impact of using this HIV clinical trial information booklet in addition to standard trial information (SI) compared with SI alone, on knowledge and understanding of the clinical trial process.

Methods

Study population

Those eligible for enrolment in the study were HIV-1 positive men and women attending the HIV clinic at the Chelsea and Westminster Hospital in west London between January 1997 and June 1998. Specific clinics

where the physicians were involved in clinical trials and known to refer patients to trials were targeted, and all patients attending that clinic were asked if they would like to join this study. A number of patients were found to be ineligible for the trial that they were considering joining, and thus did not participate in this study.

For those patients who were eligible, approximately one-third did not wish to join the study, mainly due to the number of forms they had to complete, not having the time, too ill and limited understanding of the English language. The randomization procedure involved generating a set of numbered randomization envelopes that were opened only (in numerical order) by MT or SD once the patient had agreed to participate in the study. Neither the patients nor the investigators could be blinded to the allocation arm. Patients were randomized to either SI alone or SI and the clinical trial information booklet, *Clinical Trials in HIV and AIDS: Information For People Who Are Thinking About Joining a Trial* [25]. At the Chelsea and Westminster Hospital, standard information on trials is given to each patient as part of the usual informed consent process, and consists of a patient information sheet specific to the proposed clinical trial and a discussion with the trial doctor and research nurse.

Baseline evaluation

The baseline questionnaire was designed to be self-administered, and comprised three sections.

Section A included demographic information (sex, age, nationality, ethnic group, usual spoken language, religion, educational level, current employment status and occupation); and information on HIV clinical status (date of first HIV positive test, HIV symptoms, AIDS diagnoses and most recent CD4 cell count), which was subsequently validated by MT from the patient medical records.

Section B comprised 10 questions about previous participation in clinical trials and reasons for joining/not joining; motivations and/or concerns about enrolling in the clinical trial that the patient was currently eligible to join; information about other people involved in their decision making process; the likelihood of them joining a future trial; and a self-rated assessment of their understanding of the clinical trial process.

Section C asked questions on knowledge and understanding of HIV treatments and clinical trials. The first part consisted of eight questions that were used in a National AIDS Manual survey on the treatment information needs of people living with HIV [26]. One point was awarded for each correct answer, with a maximum

possible score of eight. A further 11 multiple choice questions addressed the purpose of phase I and III clinical trials, eligibility criteria, ethics committee approval, randomization, blinding, placebos and patient rights (including informed consent issues and freedom to decline joining or to withdraw from a clinical trial). Each question had four accompanying statements that the participant could mark as 'true', 'false' or 'don't know'. Again, one point was awarded for each correct answer, with a maximum possible score of 44. This instrument was used after piloting an earlier version of eight multiple choice questions, to which the participant had either to agree or to disagree or remain undecided. However, since all patients were able to correctly answer more than half the questions in this version, 11 revised multiple choice questions were used, which were more discerning in their assessment of patient knowledge.

Follow-up evaluation

An interviewer-administered questionnaire was completed 2–6 months after randomization and completion of the baseline questionnaire. This questionnaire also comprised three similar sections.

In section A, each patient was asked to provide information about the clinical trial that he/she was currently eligible to join, including whether or not he/she had enrolled and the specific reasons for enrolling/not enrolling. The patients were also asked how carefully they had read the trial information sheet and/or the information booklet, and to assess the usefulness of these on a 10 point visual analogue scale (1 = not at all helpful and 10 = extremely helpful). They were also asked whether, during the consent process, the doctor had discussed nine specific points (trial title, purpose, design and procedures of the study, side effects, alternative treatment options, confidentiality, freedom to withdraw and right to refuse to enter a clinical trial).

Section B assessed each patient's knowledge of the protocol of the trial that he/she was eligible to join. It consisted of 13 detailed questions concerning the purpose of the trial, eligibility requirements, knowledge of the trial medication (e.g. drug names, how the drugs affect the virus, side effects and when and how to take the medication) and study design (e.g. number of visits, procedures, duration of trial and restrictions on lifestyle), with a maximum possible score of 25.

Section C involved a repeat of the 11 multiple choice questions on general knowledge of clinical trials from the baseline questionnaire.

Ethics committee approval

The local ethics committee of the Chelsea and Westminster Hospital approved the study (no. 0735).

Statistical analysis

The χ^2 , Fisher's exact and Mann-Whitney *U*-tests were used to compare baseline categorical and continuous variables, respectively, across the two groups (SI and SI plus booklet). Baseline and follow-up scores for the questions on clinical trials were compared for each group separately using the Wilcoxon matched-pairs signed rank test.

Results

Between January 1997 and June 1998, 57 patients were recruited into this study, seven of whom were subsequently excluded (four did not collect the HIV clinical trials information booklet and three failed to complete the baseline questionnaire). Therefore, 50 patients were available for analysis, of whom 27 were randomized to SI only and 23 to SI and the information booklet. The majority of patients were referred for the Agouron 1343–542 trial ($n = 35$) or the DMP 266–006 study ($n = 6$; Table 1).

Characteristics of the study patients

Table 2 summarizes the demographic and clinical characteristics of the study participants at baseline, in addition to their attitudes towards and knowledge of clinical trials. Most were homosexual men (94%), with a median age of 35 years [interquartile range (IQR) 31–42], which reflects the typical demographics of the HIV patient population attending the Chelsea and Westminster Hospital. Almost two-thirds were UK born, more than two-thirds were educated up to or beyond the UK A level and one-third were in full-time employment. However, for 18% of patients, English was not their first language. The median time since HIV diagnosis was 2.68 years (IQR 0.9–7.1), although seven patients were enrolled less than 3 months following a first HIV positive test. Fourteen (29%) patients had a previous AIDS diagnosis, and the median CD4 count at randomization was 245 cells/ μ L (IQR 188–351). There were no statistically significant differences at baseline between the two groups.

Table 1 Clinical trials enrolling at the HIV clinic, Chelsea and Westminster Hospital, between January 1997 and June 1998, to which the present study refers

Protocol and study name	Description	No. recruited to present study* (total 50)
AG1343-542 (PK), Agouron Nelfinavir Study	Phase III study comparing twice daily and three times daily dosing of NFV in combination with d4T and 3TC in HIV positive patients	35 (24)
DMP266-006, DMP Study	A 24-week phase III, multicentre, randomized, open label study to compare antiretroviral activity and tolerability of three different combination regimens (DMP266 + IDV, DMP266 + ZDV + 3TC, and ZDV + 3TC + IDV) in HIV infected patients	6 (4)
A1454-144, ddl + d4T Study	Randomized, double blind study of the antiviral activity of once daily and twice daily dosing of ddl in combination with twice daily dosing of d4T in HIV infected subjects	2
AD HOC	Randomized, double blind, placebo controlled trial to assess the efficacy and safety of adefovir dipivoxil in subjects with HIV and CD4 counts < 100 cells/ μ L	2 (1)
ANRS-079 IL-2 Study	Randomized, phase II study of subcutaneous IL-2 in addition to antiretroviral therapy (d4T/3TC/IDV) vs. antiretroviral therapy alone (d4T/3TC/IDV) in HIV positive patients with CD4 counts of 200–500 cells/ μ L	2 (1)
Kaposi's Sarcoma Study	Randomized controlled multicentre study of foscarnet treatment vs. no treatment in early HIV related Kaposi's sarcoma.	1
3TC/NVP	Phase III study to evaluate tolerance, safety and effectiveness of NVP in preventing clinical AIDS progression events or death, when used in combination with 3TC and stable background therapy	1
Remune Trial	Phase I, randomized open-label study of antiretroviral (two NRTIs and at least one PI) vs. antiretroviral therapy plus IL-2; antiretroviral therapy plus IL-2 plus Remune or antiretroviral therapy plus Remune in HIV infected subjects with CD4 counts > 300 cells/ μ L	1 (1)

*Numbers in brackets give the numbers of patients who completed follow-up for each trial (total 31).NFV = nelfinavir; d4T = stavudine; 3TC = lamivudine; IDV = indinavir; ZDV = zidovudine; ddl = didanosine; IL-2 = interleukin-2; NVP = nevirapine; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor.

Past experience and current attitudes towards clinical trials

The majority (78%) of patients had never been approached to join a clinical trial in the past. Of the remaining 11 patients, nine had been asked to join at least one trial and one patient to join six or more trials. Of these 11, seven patients had previously enrolled in a clinical trial (three in the SI group and four in the SI plus booklet group).

The two groups were similar in their self-rated assessment of their knowledge of clinical trials, their likelihood of joining a clinical trial and the reasons given for wanting to join a clinical trial (Table 2). Over 50% of the patients felt they had a 'good understanding' of clinical trials, 39% had 'some idea' and only 4% were either 'not sure' or had 'no idea'; 45 (92%) patients said they were 'highly likely' or 'likely' to join a clinical trial in the future, while only four patients were either 'undecided' or 'highly unlikely' to join a clinical trial. On motivation, 29 (69%) patients gave their main reason for joining a clinical trial as a benefit to personal health, followed by the opportunity to gain access to new treatments (17%) or to benefit others by advancing knowledge (14%). Concerns expressed about joining a clinical trial included possible drug side effects (43%), concerns about the drugs (e.g. the number of tablets, the

dosage and placebos) (25%), doubts about clinical effectiveness (5%), potential impact on long-term treatment options (5%) and possible restrictions on lifestyle (5%).

Knowledge and understanding of HIV treatments and clinical trials at baseline

The overall median score for the patients' knowledge of HIV treatments was 3/8 (IQR 1–5), and this was similar between the two groups. Twelve patients (24%) scored 0 (six in each group). Most patients knew about HIV treatments that are commonly used, for example, that saquinavir is a protease inhibitor (52%), that septrin is widely used as prophylaxis for *Pneumocystis carinii* pneumonia (55%) and that treatment with zidovudine and didanosine together is better than zidovudine alone (64%). However, few patients knew that the anticytomegalovirus drug ganciclovir was now produced in a capsule (8%), or that the risk of mother-to-child HIV transmission is reduced by taking zidovudine (17%).

The overall median score for the patients' knowledge of clinical trials was 26.5/44 (IQR 19–33), and this, too, was similar across the groups. Only four patients scored 0 (three SI and one SI plus booklet). Most patients did

Table 2 Patient characteristics at baseline

	Standard trial information (n = 27)	Standard trial information + booklet (n = 23)
Demographic information		
Median age (years, IQR)	33 (30–40)	37 (32–46)
Male	26 (96%)	21 (91%)
British nationality	17 (65%)	13 (57%)
First language English	22 (81%)	19 (83%)
Educated up to and beyond A level	19 (73%)	15 (65%)
Currently in full time employment	9 (33%)	8 (35%)
HIV clinical status		
Median duration of HIV infection (years, IQR)	3.38 (0.66–6.30)	2.68 (1.36–8.23)
Median CD4 count (cells/ μ L, IQR)	220 (190–358)	249 (166–347)
Previous AIDS diagnosis	8 (31%)	6 (27%)
Previous participation in clinical trials	3 (11%)	4 (17%)
Self-rated assessment of clinical trials knowledge		
Complete/good	16 (62%)	12 (52%)
Some/not sure/no idea	10 (38%)	11 (48%)
Likelihood of joining a clinical trial		
Highly likely/likely	25 (96%)	20 (87%)
Undecided/unlikely/highly unlikely	1 (4%)	3 (13%)
Current reasons for wanting to join a trial		
	n = 24	n = 18
To benefit personal health	16 (67%)	13 (72%)
To access new drugs	4 (17%)	3 (17%)
Altruistic	5 (21%)	1 (6%)
Current concerns about joining a trial		
	n = 23	n = 17
Drug side-effects	7 (30%)	10 (59%)
Concerns about the drugs	8 (35%)	2 (12%)
Knowledge and understanding of HIV treatments and clinical trials		
Median HIV treatment knowledge score (IQR)	4/8 (1–6)	2/8 (0–5)
Median clinical trial knowledge score (IQR)	30/44 (19–34)	23/44 (19–30)

IQR = interquartile range.

not know the purpose of phase I or III clinical trials, and only half knew the purpose of randomization, blinding and the use of a placebo. Questions about what patients should be told before they joined a trial, what would happen to their future treatment if they decide not to join the clinical trial and why they needed to sign consent forms were, in general, correctly answered. However, 46% of patients incorrectly assumed that the purpose of the consent form was to protect the doctor.

Association between patient characteristics and baseline clinical trial score

There was no association between the patients' score on knowledge of clinical trials and their sex, age, nation-

ality, ethnic origin, educational level attainment or current employment status. However, patients for whom English was not their first language scored significantly lower compared with English speaking patients [11 (IQR 0–22) vs. 29 (21–34); $P = 0.0007$], and patients with prior experience of clinical trials had a higher score than those who were joining a trial for the first time [32 (IQR 30–37) vs. 23 (17–32); $P = 0.016$]. There was also a clear association between the patients' self-assessment of their level of understanding of clinical trials and their actual score; the median score was 30.5 (IQR 24–34) for those with a 'complete or good level of knowledge' vs. 20 (12–26) for those who had 'some or no knowledge' ($P = 0.004$). We found no association between the clinical trial knowledge score and interest expressed in joining a clinical trial.

Impact of SI and the information booklet on attitudes towards clinical trials

Thirty-one patients completed the follow-up questionnaire a median of 4.7 months (IQR 2.3–31.7) following randomization (15 STI and 16 SI plus booklet); 18 patients were lost to follow-up and one was too ill to complete the follow-up questionnaire. There were no significant differences between patients who completed the follow-up and those who did not on baseline demographic characteristics (except age and employment status), stage of HIV disease, self-rated assessment of clinical trial knowledge, reasons for joining a clinical trial, and knowledge of HIV treatments and clinical trials. Compared with those who completed only the baseline assessment, the patients who completed the follow-up were significantly older [32 (IQR 28–37) vs. 38 (32–46); $P = 0.02$] and more likely to be in full-time employment (16 vs. 45%; $P = 0.02$).

Table 3 summarizes the results at follow-up in the two groups. Twenty-six (84%) patients were known to have joined one of the ongoing clinical trials (73% of SI and 94% of SI plus booklet group; $P = 0.17$). One participant was found to be ineligible for the trial following screening, one refused to enrol as he was concerned about side effects and the remaining three patients were unable to recall whether or not they had joined a trial.

These follow-up patients gave similar reasons to those cited at baseline for joining a trial. However, personal benefit to health was less commonly mentioned (42% compared with 70% at baseline). Importantly, at follow-up, patients who received the information booklet in addition to the SI were more likely to cite the benefit to personal health (63% vs. 10%; $P = 0.008$), but less likely

Table 3 Impact of the standard trial information and the information booklet on enrolment and knowledge of clinical trials and the specific trial protocol*

	Standard trial information (n = 15)		Standard trial information and booklet (n = 16)	
	Baseline	Follow-up	Baseline	Follow-up
Enrolled into a clinical trial		11 (73%)		15 (94%)
Clinical trial general knowledge score (median, IQR)	30 (19–34)	35 (27–39) [†]	24 (19.5–29)	31 (26–34) ^{††}
Specific trial protocol knowledge				
Median knowledge score (IQR)		11 (7–14)		13 (10–14.5)
Correct answers to specific questions (no., %)				
Purpose of the study		8 (53%)		8 (50%)
How do you fit the eligibility criteria?		9 (60%)		10 (63%)
What are the names of the drugs?		13 (87%)		14 (88%)
How do the drugs affect the virus?		11 (73%)		8 (50%)
What are the potential side-effects of the drugs?		11 (73%)		15 (94%)
What are the possible benefits of joining the trial?		6 (40%)		12 (75%) [‡]
How do you take the trial drug(s)?		11 (73%)		15 (94%)
What are you required to do (no visits/blood tests)?		9 (60%)		10 (63%)
How long will the trial last?		8 (53%)		9 (56%)
Are there any restrictions on your lifestyle?		4 (27%)		6 (38%)
What happens if you feel unwell whilst on the trial?		13 (87%)		15 (94%)
What should you do if you forget to take the tablets?		11 (73%)		15 (94%)
How will you find out results of the trial?		2 (13%)		4 (25%)
Reasons for joining the clinical trial	n = 13	n = 10 [§]	n = 14	n = 16
To benefit personal health	9 (69%)	1 (10%)	10 (71%)	10 (63%) ^{††}
To access new drugs	3 (23%)	3 (30%)	3 (21%)	2 (13%)
Altruistic	3 (23%)	7 (70%)	1 (7%)	4 (25%)

Baseline data are given only for patients who completed the follow-up. [†] $P = 0.0025$, ^{††} $P = 0.0022$, comparison within groups by Wilcoxon matched-pairs signed rank test; [‡] $P = 0.04$; ^{†††} $P = 0.008$, comparison between groups by χ^2 -test. [§]Five patients (in the standard trial information group) did not complete this part of the questionnaire.

IQR = interquartile range.

to cite a doctor's advice (25% vs. 70%; $P = 0.024$) as the reason for joining a trial, compared with the SI only group.

Impact of SI and information booklet on knowledge and understanding of clinical trials

The patients in both groups demonstrated a statistically significant increase in their median score from baseline (from 30 to 35/44, $P = 0.0025$, for SI only; and from 24 to 31/44, $P = 0.0022$, for SI plus booklet), and the score increase was similar for both groups [median increase of 7 (IQR 1–13) for SI only vs. 8 (3.5–9) for SI plus booklet; $P = 0.72$]. The number of patients who correctly answered each question increased for nearly every question. There were particularly marked increases in both groups in the number of patients who correctly answered the questions on phase I and III clinical trials and the purpose of blinding. We found no difference in the score or change in score for patients who had taken part in a clinical trial previously compared with those who were joining a trial for the first time.

Patient understanding of the specific clinical trial protocol

In the 13 detailed questions about the protocol of the trial that they were eligible to join, 81% of patients stated that they did not know how they would find out the results of the study, 48% of patients were unclear about the purpose of the study, 39% were unclear how they fitted the eligibility requirement, 16% did not know what to do if they forgot to take their tablets and 13% did not know the names of any of the tablets they were taking. This was despite acknowledgement that this information had been given to them in the trial information sheet and by the doctor before enrolment in the clinical trial. However, encouragingly, 84% of patients could name at least one side effect, and 90% of patients knew what to do and who to contact if they felt unwell during the trial. There was only one difference between the two groups: 75% of patients in the SI and information booklet group correctly answered the question on the possible benefits of joining the trial compared with 40% in the SI only group ($P = 0.048$). Those who had received the information booklet in addition to the SI achieved a slightly higher

score (median score 13/25) compared with those who had received only the SI (11/25), but this difference was not statistically significant ($P = 0.48$).

Assessment of the usefulness of the clinical trial information

Each patient was asked to assess the usefulness of the trial information sheet, and the information booklet if received. Most patients (94%) could recall receiving the trial information sheet, but only 69% recalled receiving the information booklet. Most (63%) said that they had read the information sheet and/or booklet 'very carefully'. The median score given by the patients for the helpfulness of the information sheet and the booklet was identical, 7/10 (IQR 5–8). Specific reasons given by patients for why they thought the information sheet and booklet were useful included being able to take the information away to read at their own leisure, having something to refer back to and the information given on what was involved if they decided to join the trial. The main reason why the SI plus booklet were considered unhelpful was that the patient had, in fact, already decided to join the trial.

The patients were also asked how useful they found the information that was provided by their doctors. They were generally satisfied with this information, giving the doctors a median score of 8.75/10 (IQR 8–9.25). For eight of the nine points that the doctor was required to discuss with the patient, 86–100% of patients felt that the doctor had covered the issues. However, only 69% of patients felt that the doctor had adequately discussed the issue of alternative treatments with them.

Discussion

In this small randomized trial, we found a comparable 7–8 point improvement in the patients' general knowledge of the clinical trial process in the group who received the SI plus the information booklet, *Clinical Trials in HIV and AIDS: Information For People Who Are Thinking About Joining a Trial* [25], as well as in those who received the SI alone. Although the 29% increase in the clinical trial general knowledge score in the SI plus information booklet group was slightly greater than in the SI alone group (17%), this did not reach statistical significance. Particular areas of knowledge that improved for both groups were the understanding of the purpose of phase I and III clinical trials and blinding. Of particular concern was the uniformly poor knowledge of the specific trial protocol details in both groups. However, despite this, the majority (84%) of our study participants (who completed follow-up) did enrol in the clinical trials for which they were eligible, and this was

slightly greater in the SI and information booklet group (94%) compared with the SI alone group (73%).

Several reasons may explain both the lack of a more dramatic impact of the comprehensive information booklet on patient understanding of clinical trials and the continuing poor level of knowledge of specific trial protocols despite the detailed information sheet. First of all, only 69% of patients could recall receiving the information booklet, and only 63% admitted that they had read the booklet and/or information sheet 'very carefully'. Second, some patients already had a relatively high level of knowledge of clinical trials at baseline (score 26.5/44), even though only a few had previously taken part in a clinical trial, and also had ready access to alternative sources of information on clinical trials throughout the follow-up period. Importantly, our sample size (initial target was 200 patients) was limited by: poor recruitment, reflecting a downturn in the number of antiretroviral drug trials recruiting during the study period; delays in starting recruitment to three of the trials due to protocol amendments; and a 38% loss to follow-up rate. A further concern was a delay in administering the follow-up questionnaire in 39% of study participants who completed follow-up, which may have led to an impaired recall of the details of the trial protocol. However, we found no difference in the median score for knowledge of either clinical trials or the trial protocol in those followed up within 3 months and those interviewed later.

Factors that were unlikely to have contributed to the lack of impact of the information booklet include the quality of the information sheet and booklet. The information sheet and booklet were considered equally helpful, although patients were most satisfied by the information provided by their doctor. Most patients commented that it was useful to take the information sheet and booklet away to read at their own leisure and to have something to refer back to. Similarly, the poor knowledge of the specific trial protocol cannot be explained by a low level of trial enrolment, whereby patients who elected not to join would be less likely to recall details of a study. In this study, the majority of patients (84%) joined the clinical trial for which they were eligible, which contrasts with findings from other studies [3,4,6]. The probable reason for this high level of enrolment is that only patients who were eligible for or already considering joining a trial were invited to participate in our study. Furthermore, at baseline, 92% of patients said that they were either 'highly likely' or 'likely' to join a clinical trial and a number of patients stated that the information sheet and booklet were not particularly useful, as they had already decided to join the trial. Therefore, the patients who agreed to join this study may represent a

biased subset of patients who were more likely to join a clinical trial anyway.

The poor recall of the specific trial protocol details is of particular concern. Areas where a high proportion of respondents gave incorrect answers included the purpose of the study, eligibility criteria and what to do if they forget to take their tablets. However, patients in our study are not unique in their lack of knowledge about the clinical trial that they are eligible to join. A similarly poor understanding or recall of information about surgical procedures or medical therapies has been reported when standard informed consent approaches of verbal and written information have been used. In a 1987 survey of 100 patients following surgery, 27% did not know which organ had been operated upon, and 44% were unaware of the basic facts relating to the operation [13]. Similarly, of 100 patients undergoing chemotherapy who had received written information and a consent form, 75% could not name any of the chemotherapy drugs and 61% could not remember the number of drugs they had received [14]. In contrast, in a smaller study of 39 hypertensive patients enrolled in a trial comparing the antihypertensive effectiveness of two drugs, patients had a good recall of information, with an average score of 71.6% and 61.2% at 2 h and 3 months after enrolment, respectively [27]. Another study comparing total disclosure of information to the patient vs. an individualized approach (whereby the consultant decided how much information the patient received) reported patients in the total disclosure group to be more knowledgeable shortly after signing the consent form, about the possible treatment side effects and the research nature of the study [28]. However, it is less encouraging that patients in the total disclosure group were also more anxious and less willing to participate in the trial compared with patients in the individualized approach group.

To our knowledge this is the first study to investigate the use of an information booklet to improve patient knowledge of the clinical trial process. Use of other supplementary educational materials and approaches, such as videos, computers and teaching sessions, to improve patient understanding of the informed consent process in other areas has, in general, been disappointing. In a randomized trial of cancer patients' understanding of a hypothetical study, no difference was found between those patients who received information by audio tape or by computer on the day following the intervention [19]. There was also no difference in the level of knowledge between patients who received written information about electroconvulsive therapy and those who also watched a video [21]. However,

this was a small study of only 18 subjects, 11 of whom were randomized to the video arm, and so the results are inconclusive. In contrast, in a randomized comparison of discussion alone vs. video alone vs. discussion plus video in improving 201 patients' understanding of colonoscopy procedures, the use of the video was associated with a significantly improved knowledge level [18].

The reasons given by patients for having joined or considering joining a clinical trial were similar to those reported elsewhere: benefits to personal health [12,29,30], access to new treatments [12] and altruistic motives [10,29–31]. An apparent benefit of the information booklet was to alter patients' reasons for joining the trial, with those who also received the booklet more likely to cite 'benefit to personal health' as their reason for joining the trial. What is evident is that while patients do realize the need for well designed clinical trials to advance medical science and develop better treatments, they are less keen on personally taking part in a clinical trial [29,31]. In a questionnaire based study that assessed patients' attitudes to receiving an HIV preventative vaccine, 91% of patients wanted to be given such a vaccine after it had been developed, but only 22% of patients said that they were 'extremely likely' to participate in such a trial [31].

We also asked patients about their concerns regarding clinical trials, which included side effects (34%) and concerns about the study drugs, including the number and dosage of tablets (14%), which is similar to the findings of other surveys; 25% of 133 patients attending an HIV clinic stated possible side effects as their main reason for not joining a trial [12], as did 28% of 200 gay/bisexual men [31]. In studies of cancer, palliative, cardiology and HIV patients, other reasons for not enrolling include concerns about placebo studies [6,12,31], wary of or unable to give informed consent [5,6], the fear of being a 'guinea pig' [5,12,31], too unwell [6,11], financial considerations [4,10,31] and too time consuming [10–12].

Our failure to show a clear additional benefit of a comprehensive information booklet on the likelihood of patients enrolling in or understanding clinical trials or having knowledge of the specific trial protocol may be attributable in part to the low percentage of patients who carefully read the information provided. The booklet was 16 pages, and took approximately 30 min to read. We have now developed a video [32], which more succinctly presents the same information. Further evaluation will be needed to assess the impact of this approach. However, it is clear that investment of time by a well-informed and sympathetic doctor and/or nurse will remain the mainstay of the informed consent process.

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