

Awareness of Clinical Trials Participation among Healthy Volunteers

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Abstract--Clinical trials (CTs) are important part of improving quality of health care. However, recruitment is a major challenge for many trials globally. Likewise, in Malaysia one study that focused on the barriers to CTs participation found that patient participation in cancer CTs is extremely low. Various factors were identified including lack of transportation, lack of interest, job commitment, and medical problems. Nevertheless, until today no study has been conducted to examine the awareness of participation among healthy volunteers. Hence, this study aimed to investigate the reasons why individuals' wish and wish not to participate in CTs. A case study survey design was used for data collection and analysis of randomly selected staff and students of Universiti Utara Malaysia. A questionnaire was developed to derive effective outcomes based on literature review. Of 2066 participants invited to take part in the survey, 927 (45%) filled the questionnaire. Most of the participants had never participated in a CT (97.2%). The majority of the population was female, aged 18 to 24 years, well educated, and aware of CT from internet. Only 358 (2-6.9%) participants would definitely participate in CT compared to 482 participants who chose possibly and 87 chose never to participate. Low understanding of CT was the main reason that made them to be hesitant whether or not to participate in CT. The majority (36.6%) were motivated to participate to improve personal health aspects. However, fear of risks or complication involved in CT was the main reason (20.2%) that reduced their motivation to participate. The results of this study revealed that younger population have awareness of CT but chose not to participate. Knowledge and a sound understanding of CT is required to motivate their participation in future.

Key words--Awareness, participation, clinical trials, healthy volunteers, participate.

I. INTRODUCTION

Clinical trials (CTs) are an important part of improving quality of health care. However, recruitment of sufficient trial participants is not easy, and it is a continuing problem faced by drug companies wishing to test new drugs [1]. The general public and patients are still not fully aware of the importance of participation in CTs for the development and implementation of medical devices [2]. Without an adequate number of participants enrolled, a trial will not be able to answer the questions about the benefits and risks of a new therapy [3]. Low participation rates can also threaten the depletion of study financial resources; this often forces the doctors albeit investigators to

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extend the period of recruitment, add incentives and recruitment personnel, and otherwise struggle to meet recruitment targets [4]. Studies that are not successful in overcoming these challenges are likely to be under-powered or fail to achieve statistical significance due to inadequate recruitment. In a recent study by Oregon Health Sciences University researchers, one third of all studies terminated between 2005 and 2009 at OHSU had low recruitment (zero to one participant), costing the institution nearly \$1 million annually [5].

Similarly, a study of oncology clinical trials revealed that over half of the studies reviewed closed prematurely due to low recruitment [6]. Simply put, there is great pressure to recruit an adequate number of participants and to do so quickly to determine the success of a trial. As such, it is not surprising that studies have been conducted on why we should sometimes allow doctors to pressure patients to participate in CT [7].

Patient recruitment in Malaysia is not a potential problem as there is a large pool of patients available [8]. However, one study that focused on the barriers to CT participation found that patient participation in cancer CT is extremely low. Various factors were identified including lack of transportation, lack of interest, job commitment, and medical problems [9]. Nevertheless, until today no study has been conducted to examine the reasons why healthy volunteers wish not to participate in such trials. It is important to note that apart from patients, CTs also require healthy volunteers to participate as subjects. Declaration of Helsinki provides that, "The subjects should be volunteers – either healthy volunteers or persons or patients from whom the experimental design is not related to the patient's illness." Phase I studies, for example are conducted on healthy volunteers to determine the absorption, excretion and safety of new drugs. This is partly because the patients may have impaired organ function, and thus will not give a true picture of drug metabolism. As the clinical validity of treatments are often established by CTs, being aware of why people are willing or reluctant to participate in such studies would enable doctors albeit researchers to overcome barriers and develop better processes for recruitment rates. With an improved healthcare system, the public would definitely benefit in the end. Hence, this study aims to examine the awareness to participation in CTs among the healthy volunteer specifically the staff and students of Universiti Utara Malaysia.

II. METHODOLOGY

This study employed a survey involving students and staff of Universiti Utara Malaysia as a case study. The questionnaire was developed with three categories to derive effective outcomes based on literature review. The categories were the background information, knowledge of CT and barriers to participation to achieve the objectives of the study. Three experts in CT field reviewed the survey and provided their feedback. The survey was revised according to all the inputs.

Awareness of CT was measured by asking "What is your understanding about clinical trials?" Participants were given the following three choices: none, low, moderate and high. Participants were also asked "How would you best describe clinical trials?" Participants were given the following three choices: A last ditch effort at finding a treatment, which poses significant risk to trial participants; A way of doctors finding out whether a treatment works in people and if it has greater benefits than other treatments; and A way for doctors to provide better, new treatments for their patients. Participants were also asked "How do you know about clinical trials?" Participants were given the

following five choices regarding the sources from which they obtained information about clinical trials: from your doctor; media/advertisement; friends/relatives; internet; and education institution.

We also assessed any previous experience with CT by asking “Have you participated in clinical trial(s)?” “If yes, would you participate in future trials?” and “Do you have any recommendations for improvement?” The question about willingness to participate in clinical trials was measured using an 11-point Likert scale by asking “Would you like to participate in clinical trials?” Scores of 0- never, 5 - possibly, and 10 - definitely were assigned to correspond with never, possibly and definitely. Participants were also asked “Do you think that your health state (for example if you had a chronic illness) would affect your willingness to participate in a clinical trial? Please elaborate.”

Participants were asked to consider ten items related to the question “How important would each of these reasons be in your decision to participate in clinical trial?” to measure the factors associated with willingness to participate in clinical trials. These were: improve the health of future generations; support health research; improve personal health; benefit from additional care; access to new treatments; access further information about condition; doctor’s recommendation; attractive reimbursement for participation; limited treatment options; and expectations of effectiveness of new drugs. Participants were also asked to consider seven items following the question: “How important would each of these reasons be in your decision not to participate in clinical trial?” These items were: not assured of being allocated to the trial drug group; no certainty that the treatment will work; fear of risks or complication involved in clinical trial; lack of trust in the clinical trial; dislike paperwork; religious objections; and participation is too time-consuming or inconvenient.

Descriptive statistics of participants’ demographics, awareness of CT and willingness to participate in CT were analyzed. Associations among the variables were evaluated by chi square test, independent t-test, or one-way ANOVA. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 23.0 with a level of significance of $p < .05$.

III. RESULT

2066 invitations were sent to students and staff of Universiti Utara Malaysia to participate in a survey. Of this, 927 (45%) participants completed the questionnaire. The majority of participants were females (73.14%), aged 18 to 24 years (63.5%), Malay (84.3%) and currently studying towards a degree (65.4%). The demographic data of the 927 participants are shown in Table 1.

Table 1: Demographic data of 927 participants

Profile		Frequency	Percent
Age	18 to 24 years	589	63.5
	25 to 34 years	158	17.0
	35 to 44 years	130	14.0
	45 to 54 years	43	4.6
	55 to 60 years	5	.5
	Above 60 years	2	.2
Gender	Male	249	26.9

	Female	678	73.1
Race	Malay	781	84.3
	Chinese	87	9.4
	Indian	43	4.6
	Others	16	1.7
Are you towards a	Yes	606	65.4
	No	321	34.6
What is of	Primary School	3	.3
	Secondary	136	14.7
	University	338	36.5
	Diploma	130	14.0
	Others	320	34.5

Most of the participants best describe CT as a way for doctors to provide better, new treatments for their patients to (65.7%) followed by a way of doctors finding out whether a treatment works in people and if it has greater benefits than other treatments (30.2%) and a last ditch effort at finding a treatment, which poses significant risk to trial participant (4.1%). Of 927 participants, 430 (46.4%) reported that they knew about CT from internet, followed by 269 (29.0%) media and 126 (13.6) education institution. Majority of the participants had never participated in a CT (97.2%). Out of 26 (2.80%) participants who participated, 20 (76.92%) participants would like to participate again in future (76.92%). When asked if they have any recommendation for improvements, most of the participants thought that knowledge of CT is required to motivate participation as well as to increase awareness of CT. [Table 2]

Table2: Knowledge of clinical trials

		Freque	Percent
How would you best describe clinical trial?	A last ditch effort at finding	38	4.1
	treatment, which poses		
	risk to trial participant.		
	A way of doctors finding out	280	30.2
	whether a treatment works in		
	people and if it has greater		
	benefits than other		
	A way of doctors to provide	609	65.7
	new treatments for their		
How do you know clinical trials?	From your doctor	32	3.5
	Media	269	29.0
	Friends	70	7.6
	Internet	430	46.4
	Education institution	126	13.6
Have you participated clinical trial(s) before?	Yes	26	2.8
	No	901	97.2

When asked about their understanding towards CT, 423 participants agreed that the level of understanding is low. 272 (64.3%) participants were aged 18-24 years followed by 1 (0.2%) participant aged 55-60 years and 1

participant aged more than 60 years. Result showed also that 119 (28.1%) participants were males and 304 (71.9%) participants were females with 355 (83.9%) participants were Malay followed by 44 (10.4%) participants Chinese, 15 (3.55) participants was Indian and 9 (2.1%) others [Table 3].

Table 3: Background of participants (age, gender and race) on knowledge about clinical trials

What is your understanding about clinical trials?						
		None	Low	Moderate	High	Total
Age	18 to 24 years	127	272	187	3	589
		71.3%	64.3%	58.6%	42.9%	63.5%
	25 to 34 years	26	72	58	2	158
		14.6%	17.0%	18.2%	28.6%	17.0%
	35 to 44 years	18	60	50	2	130
		10.1%	14.2%	15.7%	28.6%	14.0%
	45 to 54 years	5	17	21	0	43
		2.8%	4.0%	6.6%	0.0%	4.6%
	55 to 60 years	2	1	2	0	5
		1.1%	.2%	.6%	0.0%	.5%
	Above 60 years	0	1	1	0	2
		0.0%	.2%	.3%	0.0%	.2%
		178	423	319	7	927
	Total	100.0%	100.0%	100.0%	100.0%	100.0%
Gender	Male	42	119	85	3	249
		23.6%	28.1%	26.6%	42.9%	26.9%
	Female	136	304	234	4	678
		76.4%	71.9%	73.4%	57.1%	73.1%
	Total	100.0%	100.0%	100.0%	100.0%	100.0%
Race	Malay	137	355	283	6	781
		77.0%	83.9%	88.7%	85.7%	84.3%
	Chinese	29	44	13	1	87
		16.3%	10.4%	4.1%	14.3%	9.4%
	Indian	7	15	21	0	43
		3.9%	3.5%	6.6%	0.0%	4.6%
	Others	5	9	2	0	16
		2.8%	2.1%	.6%	0.0%	1.7%
	Total	178	423	319	7	927
		100.0%	100.0%	100.0%	100.0%	100.0%

When asked would you participate in a CT by given scale 0 – 10 where 0 – never, 5 – possibly and 10 – definitely, majority participants chose possibly with 482 (52%) followed by never (level 0) which composed of 87

(9.4%) and definitely is between 2% to 6.9% with overall mean is 4.54 (SD=2.233). [Table 4].

Table 4: Participants' willingness (never, possibly, definitely) on participation in a clinical trial

		Frequency	Percent	Mean	Std. Deviation
Would you participate in a clinical trial? (11-point scale)	0	87	9.4	4.54	2.233
	1	33	3.6		
	2	50	5.4		
	3	38	4.1		
	4	64	6.9		
	5	482	52		
	6	57	6.1		
	7	39	4.2		
	8	33	3.6		
	9	19	2		
	10	25	2.7		
	Total	927	100		

Next, when asked "Do you think that your health state (for example if you had a chronic illness) would affect your willingness to participate in a CT, only 462 (47.53%) participants answered the question with 271 (58.66%) participants answered in affirmative followed by 104 (22.51%) participants answered 'no' and 85 (18.4%) participants answered 'not sure'. [Table 5].

Table 5: List of answers given by participants saying that they are not willing to participate if had a chronic illness

No.	Answers
1.	"It will affect my willingness to participate as it may worsen my health condition."
2.	"It creates the fear of risk of the complication of the clinical trial."
3.	"I'd feel hesitate if the clinical trial could result in something unpleasant to my current health."
4.	"No. not willing to take the risk."
5.	"No. I won't participate in a clinical trial because I'm a bit scared of medicine."
6.	"Being sick is hard enough and to participate in this would add up my hardship."
7.	"Because the procedure might be uncomfortable."
8.	Tidak. Membebaskan."
9.	"Walauapapun yang terjadipadakesihatansaya, sayatidaksanggupmenjadibahanujikajimakmalpenyelidikanklinikal."

Next, when asked “Do you think that your health state (for example if you had a chronic illness) would affect your willingness to participate in a CT, only 462 (47.53%) participants answered the question with 271 (58.66%) participants answered in affirmative followed by 104 (22.51%) participants answered ‘no’ and 85 (18.4%) participants answered ‘not sure’.

Table 6 shows that from 5 variables (*age, gender, race, income and highest qualification*) to see the difference between two variables that is profile and participants’ willingness to participation, only *race* is significant ($p = 0.000$). Meanwhile Table 7 shows that *age* ($p = 0.018$) and *race* ($p = 0.012$) are significant between two variables that is profile and participants’ willingness not to participation.

Table 6: Participants’ willingness (age, gender, race, income, level of education) to participate (N=927)

	Profile	Frequency	Percent	p	
Age	18 to 24 years	589	63.5	.446	Anova
	25 to 34 years	158	17.0		
	35 to 44 years	130	14.0		
	45 to 54 years	43	4.6		
	55 to 60 years	5	.5		
	Above 60 years	2	.2		
Gender	Male	249	26.9	.967	T-Test
	Female	678	73.1		
Race	Malay	781	84.3	.000	Anova
	Chinese	87	9.4		
	Indian	43	4.6		
	Others	16	1.7		
	RM0 - RM12000	785	84.7	.240	Anova
	RM12001	51	5.5		
	RM24001	40	4.3		
	RM40001	33	3.6		
	Over RM60000	18	1.9		
What is your highest level of education to date-	Primary School	3	.3	.549	Anova
	Secondary	136	14.7		
	University	338	36.5		
	Bachelor's				

Table 7: Participants’ willingness not (age, gender, race, income, level of education) to participate (N=927)

	Profile	Frequency	Percent	p	
Age	18 to 24 years	589	63.5	.018	Anova
	25 to 34 years	158	17.0		
	35 to 44 years	130	14.0		
	45 to 54 years	43	4.6		
	55 to 60 years	5	.5		
	Above 60 years	2	.2		

Gender	Male	249	26.9	.985	T-Test
	Female	678	73.1		
Race	Malay	781	84.3	.012	Anova
	Chinese	87	9.4		
	Indian	43	4.6		
	Others	16	1.7		
	RM0 - RM12000	785	84.7	.183	Anova
	RM12001 - RM24000	51	5.5		
	RM24001 - RM40000	40	4.3		
	RM40001 - RM60000	33	3.6		
	Over RM60000	18	1.9		
What is your highest level of education to date-	Primary School	3	.3	.643	Anova
	Secondary School	136	14.7		
	University Bachelor's Degree	338	36.5		

The factors that were directly associated with improved participation within CT are given in Table 8. Majority of the participants agreed that all 10 items given in the questionnaire gave a good impact on them to participate in clinical trials: improve the health of future generations (45.3%), support health research (49.7%), improving personnel health (43.9%), benefit from additional care (49.3%), access to new treatments (45.2%), access further information about condition (49.2%), doctor's recommendation (46.4%), attractive reimbursement for participation (34.6%), limited treatment option (37.8%) and expectation of effectiveness of new drugs (39.8%). However, of 10 items developed to see the motivation to participate: to improve personal health was the most important factor with 339 participants agreeing with the statement (36.6%; mean=4.1316; SD=0.82741) followed by to improve the health of future generations of 307 participants (33.1%; mean=4.0647; SD=0.84687) and access to new treatments of 286 participants (30.9%; mean=4.0248; SD=0.83810).

Table 8: Motivating factors to participate in clinical trials

How important would each of these reasons be in your decision to participate in clinical trial?	Scale	Frequency	Percent	Mean	Std. Deviation
Improve the health of future generations	No Impact	10	1.1	4.0647	.84687
	Small Impact	27	2.9		
	Moderate	163	17.6		
	Good	420	45.3		
	Large Impact	307	33.1		
Support health research	No Impact	9	1.0	4.0076	.83326
	Small Impact	35	3.8		
	Moderate	159	17.2		

	Good	461	49.7		
	Large Impact	263	28.4		
Improve	No Impact	11	1.2	4.1316	.82741
personnel health	Small Impact	14	1.5		
	Moderate	156	16.8		
	Good	407	43.9		
	Large Impact	339	36.6		
Benefit from	No Impact	9	1.0	4.0345	.79747
additional care	Small Impact	16	1.7		
	Moderate	177	19.1		
	Good	457	49.3		
	Large Impact	268	28.9		
Access to new	No Impact	10	1.1	4.0248	.83810
treatments	Small Impact	21	2.3		
	Moderate	191	20.6		
	Good	419	45.2		
	Large Impact	286	30.9		
Access further	No Impact	9	1.0	4.0108	.81289
information	Small Impact	23	2.5		
about condition	Moderate	178	19.2		
	Good	456	49.2		
	Large Impact	261	28.2		
Doctor's	No Impact	17	1.8	3.8846	.87973
recommendation	Small Impact	32	3.5		
	Moderate	220	23.7		
	Good	430	46.4		
	Large Impact	228	24.6		
Attractive	No Impact	32	3.5	3.4951	.97025
reimbursement	Small Impact	82	8.8		
	Moderate	350	37.8		
for participation	Good	321	34.6		
	Large Impact	142	15.3		
Limited	No Impact	19	2.0	3.5663	.89616
treatment option	Small Impact	63	6.8		
	Moderate	357	38.5		
	Good	350	37.8		
	Large Impact	138	14.9		
Expectation of	No Impact	11	1.2	3.7713	.88026
effectiveness of	Small Impact	40	4.3		
new drugs	Moderate	303	32.7		
	Good	369	39.8		
	Large Impact	204	22.0		

Majority of the participants agreed that all 7 items developed in the questionnaire gave moderate impact on them not to participate in CT: Not assured of being allocated to trial drug group (48.3%), No certainty that the treatment will work (42.2%), Fear of risks or complication involved in CT (35.9%), Lack of trust in the CT (46.7%),

Dislike paperwork (45.8%), Religious objections (42.1%) and Participation is too time-consuming or inconvenient (44.3%). Meanwhile, the most significant factors that discouraged participation were fear of risks or complication involved in CT with large impact of 187 participants (20.2%; mean=3.5890; SD=0.98059) followed by no certainty that the treatment will work of 123 participants (13.3%; mean=3.3581; SD=0.97101) and participation is too time-consuming or inconvenient of 117 participants (12.6%; mean=3.3333; SD=0.97374). [Table 9]

Table 9: Reasons that would discourage participants from participating

How important would each of these reasons be in your decision not to participate in clinical trial?	Scale	Frequency	Percent	Mean	Std. Deviation
Not assured of being allocated to trial drug group	No Impact	36	3.9	3.2751	.92881
	Small Impact	105	11.3		
	Moderate	448	48.3		
	Good	244	26.3		
	Large Impact	94	10.1		
No certainty that the treatment will work	No Impact	29	3.1	3.3581	.97101
	Small Impact	120	12.9		
	Moderate	391	42.2		
	Good	264	28.5		
	Large Impact	123	13.3		
Fear of risks or complication involved in clinical trial	No Impact	19	2.0	3.5890	.98059
	Small Impact	89	9.6		
	Moderate	333	35.9		
	Good	299	32.3		
	Large Impact	187	20.2		
Lack of trust in the clinical trial	No Impact	38	4.1	3.2686	.94795
	Small Impact	114	12.3		
	Moderate	433	46.7		
	Good	245	26.4		
	Large Impact	97	10.5		
Dislike paperwork	No Impact	54	5.8	3.0971	.97333
	Small Impact	162	17.5		
	Moderate	425	45.8		
	Good	212	22.9		
	Large Impact	74	8.0		
Religious objections	No Impact	130	14.0	2.8511	1.11123
	Small Impact	182	19.6		
	Moderate	390	42.1		
	Good	146	15.7		
	Large Impact	79	8.5		

Participation is too time-consuming or inconvenient	No Impact	38	4.1	3.3333	.97374
	Small Impact	105	11.3		
	Moderate	411	44.3		
	Good	256	27.6		
	Large Impact	117	12.6		

IV. DISCUSSION

This study revealed that most of the participants had never participated in a CT (97.2%). However, majority of the participants have awareness about CT where of 927 participants, 430 (46.4%) participants reported that they knew about CT from internet, followed by 269 (29.0%) media and 126 (13.6) education institution. This finding is not surprising since majority of the participants is composed of younger population aged between 18 to 24 years old and currently studying towards a degree.

Nevertheless, awareness did not translate into willingness to participate where only 358 (2-6.9%) participants reported that they would definitely participate in CT compared to 482 (52%) participants would possibly and 87 (9.4%) participants would never to participate. This finding seems to be consistent with one study that indicated a belief in the importance of CT, but limited understanding of the trial process persists [10]. Yet, this finding does not indicate that the participants are not interested in participating in the CT. Many of them expressed that they would like more information about CT before making decision about whether to participate. The lack of knowledge or understanding of CT serves as the reason why participants are reluctant or hesitate to participate in CT (423 participants) [Table 3]. As said by one expert from UKM Medical Centre, “The advantages or benefits that can be gained from participation are relatively unknown to patients in particular and the Malaysian society in general. Therefore, due to this lack of knowledge, CT are seen as something negative. People in the past thought that the purpose of doctors albeit researchers conducting CT is to 'dabble' and be harmful to patients who are akin to guinea pigs in scientific world.” [11]. This finding also corresponds with several studies that showed the participants were interested in participating in CT but lack adequate information was a common factor [12] [13].

Interestingly, the majority of participants considered improving personal health as the most important factor to participate in a CT. Only 142 (15.3%) participants considered attractive reimbursement for participation as the most important factor for participation. Conversely several studies showed that the main reason for healthy volunteers' willingness to participate is because of the financial reward [14] [15] [16] whereas the main reasons for patients to participate in CT is for self-interest in terms of health benefits [17] [18]. Also, the study shows that the doctor's recommendation with 228 (24.6%) participants was not the main reason to participate in CT. In contrast, one study revealed that healthy volunteers participated without knowing many things about the trial and it was noticed that their participation was only based on trust in the doctor [19]. Recently, another study also revealed that participants are more likely to participate based on trust in the doctor [20].

Meanwhile, the most significant factors that discouraged participation were fear of risks or complication involved in CT with 187 participants (20.2%; mean=3.5890; SD=0.98059) indicating so. This finding seems to be consistent with the finding of several studies that have shown that risk serve as a barrier to participation in CT

among the healthy volunteers [21] [22] [23]. This study also revealed that health state for example if participants had a chronic illness would affect their willingness to participate. Of 462 (47.53%) participants answered, 271 (58.66%) participants answered in affirmative that health state would affect their willingness to participate followed by 104 (22.51%) participants answered 'no' and 85 (18.4%) participants answered 'not sure'. A possible explanation for this discrepancy is that this present study result comes from a hypothetical question. Perhaps the participations would make a different choice if they were face with a real life situation.

This study focused on staff and students of University Utara Malaysia, a public university in northern part of Malaysia as a case study to investigate the awareness and factors associated with their willingness to participate in CT. A nationwide survey study on broader population may be more revealing on investigating the barriers to participation in CT and thus should be a logical extension of this research.

V. CONCLUSION

Although Malaysia does not have a problem to recruit sufficient number of patients to participate in CT; the situation is different in the recruitment of healthy volunteers. Knowing the reasons why people are willing or reluctant to participate in CT would enable doctors to overcome barriers and work on positive factors to improve recruitment rate. In addition, knowing the reasons for the willingness of an individual to participation is vital because CT involve risks that could pose a danger to himself for the sake of offering benefits to future patients. Hence, it is important to bring about knowledge and a sound understanding of CT specially among the public because it is an ethical imperative to increase knowledge and understanding so that voluntary, educated, and informed decision-making would be possible on his/her part as well as to motivate participation in future.

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