



## WILLINGNESS TO PARTICIPATE IN SOUTH AFRICAN HIV VACCINE TRIALS — CONCERNS OF MEDICAL PROFESSIONALS IN THE WESTERN CAPE

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**Objectives.** To evaluate the willingness of medical doctors working at a tertiary hospital to participate in HIV vaccine trials, their perceptions of patients' willingness to participate, and the major reasons underlying these views.

**Design.** A self-administered, anonymous postal survey conducted in two rounds between May and July 2001.

**Setting.** A tertiary care hospital in the Western Cape.

**Subjects.** All medical doctors listed on the hospital's staff directory.

**Outcome measures.** Willingness to participate in, and to recruit patients into, HIV vaccine trials, and the reasons for this.

**Results and conclusions.** Of the 289 individuals surveyed, 80% stated either that they would not be willing to participate in HIV vaccine trials or that they were unsure about their participation. Meanwhile, 37% stated that they would be willing to recruit patients into vaccine trials. The most common concerns with trial participation were the possibility of vaccine-induced infection and the possibility of testing positive for antibodies to HIV. The surprisingly low level of willingness to participate in trials in this sample of medical professionals highlights the importance of preparatory work to overcome substantial barriers to HIV vaccine trial participation.

*S Afr Med J* 2002; 92: 904-906.

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HIV vaccine trials are being planned in South Africa, and large-scale phase III trials are likely to begin in the next few years. While South Africa is considered an 'ideal' venue for HIV vaccine trials because of its relatively high HIV seroprevalence, it is likely that local vaccine trials will be fraught with misperceptions and numerous barriers to trial participation,<sup>1</sup> with individuals' willingness to participate in trials influenced by the provision of accurate and appropriate information addressing their fears and concerns.<sup>2</sup> Despite the growing body of evidence demonstrating the importance of perceptions of HIV vaccines in shaping the decision to participate in trials,<sup>3,4</sup> there have been no published data from South Africa on (mis-)perceptions of HIV vaccines, or on the willingness of different South African populations to participate in vaccine trials.

The willingness of medical doctors to participate in vaccine trials is particularly important, both because doctors represent a high-risk potential study population (given their occupational exposure to HIV), and because doctors and other health care workers are likely to be important 'gatekeepers' involved in shaping community norms as well as recruiting patients into HIV vaccine trials. If medical doctors are unwilling to be involved in HIV vaccine studies, this may present a significant barrier to trial recruitment. We undertook a survey to document the willingness of medical doctors working in a tertiary hospital to participate in HIV vaccine trials, their willingness to recruit patients as trial participants, and the reasons underlying these decisions.

### METHODS

A self-administered postal survey was conducted at a tertiary care hospital in the Western Cape between May and July 2001. A list of all medical doctors working at the hospital ( $N = 488$ ) was obtained from the provincial and hospital administration. The survey comprised two rounds – a first mailing, and then a second mailing sent to those who did not respond to the first mailing.

The documents sent out to each participant in the first mailing contained a covering letter explaining the purpose of the study, who the researchers were, and the process that would be followed regarding responses together with a three-page questionnaire. The completed, anonymous questionnaire was to be sent back in a blank envelope enclosed in a second, coded outer envelope. All returned envelopes were processed by an independent third party, blinded to the study purpose, who checked the envelopes received against the original mailing list. The third party then sent a second mailing to all non-responders, again without the researchers being aware of respondents' identities.<sup>5</sup> After the second round was completed, 344 responses were received (a 70% overall response rate); 289 were valid responses, and the remaining 55



were the result of invalid addresses (most of whom were no longer employed at the hospital).

The questionnaire itself contained two questions on respondents' willingness to participate in phase I HIV vaccine trials as healthy volunteers — the first and last questions of the survey instrument. The remaining questions investigated willingness to recruit their patients into vaccine trials (phase III), and the reasons underlying participants' statements. All questions referred to the hypothetical use of a DNA subunit vaccine, not a live attenuated vaccine.

Data were analysed using SAS version 8.0 (SAS Corporation, Cary, USA). We dichotomised participant age into less than or equal to 40 years (versus over 40 years) of age; the proportion of time spent in clinical practice was divided into part-time clinical practice (less than 75% of time spent seeing patients) versus active clinical practice (more than 75% of time spent with patients). Chi-square and Fisher's exact tests were used to test for differences between proportions. Multiple logistical regression was used to test associations after adjustment for various participant characteristics; such adjustments did not alter the study results substantially, and as a result the unadjusted associations are reported here. Ethical approval for the study was provided by Subcommittee C, the Research Ethics Committee of the Faculty of Health Sciences, University of Stellenbosch.

**RESULTS**

Table I describes the demographic and professional characteristics of the 289 physicians responding to the survey. The first question of the survey investigated subjects' willingness to participate in HIV vaccine trials. Twenty per cent of respondents (*N* = 58) stated that they would be willing to participate, 39% (113) indicated that they would not participate, and 41% (118) said they were unsure. Female doctors were significantly less likely to be willing to participate compared with male doctors (*P* = 0.001). Of the physicians who expressed willingness to participate, most (76%, *N* = 44) gave as their motivation concern over the magnitude of the HIV pandemic and the urgency of finding a solution via scientific research.

The concerns associated with possible vaccine trial participation are shown in Table II. Of those surveyed, 81% (*N* = 234) cited the potential for vaccine-induced infection as a major barrier to participation. Testing HIV-positive due to serological response after vaccination was cited as a concern by 68% of respondents, and was cited more often by female doctors, younger doctors, and doctors in active clinical practice (*P* = 0.07, 0.007 and 0.035, respectively). In addition, 59% of the sample indicated that concern about the effect of testing HIV-positive on their medical careers was a barrier to trial participation. This was more often a concern of younger doctors (with 73% of young doctors versus 55% of older

**Table I. Participant demographic and professional characteristics**

Characteristic	Number ( <i>N</i> = 289)	Percentage*
Age (yrs)		
21 - 30	67	23
31 - 40	119	41
41 - 50	58	20
51 - 60	38	13
> 60	6	2
Gender		
Female	95	33
Male	190	67
Professional title		
Consultant	119	41
Registrar	113	39
Medical officer	26	9
Community service	6	2
Other (including interns)	21	7
Fraction of time spent in clinical practice (%)		
≤ 25	38	13
26 - 50	32	11
51 - 75	77	27
≥ 76	138	48

\*Percentages may sum to slightly more or less than 100 due to rounding.

**Table II. Specific concerns regarding HIV vaccine trials among the 289 responding physicians**

	Number noting concern/number responding to item*	Percentage
<b>Concerns regarding physicians' own participation</b>		
Potential of vaccine to cause infection	220/271	81
Insurance/bond application denial	209/265	79
Testing HIV-positive without being infected	193/268	72
Effectiveness of vaccine	171/256	67
Effect of testing HIV-positive on medical career	193/256	75
Possibility of receiving placebo and not vaccine	72/248	29
Other	47/125	38
<b>Physicians' perceptions of patients' concerns</b>		
Potential of vaccine to cause infection	273/277	99
Testing HIV-positive after vaccine	242/267	91
Effectiveness of vaccine	225/256	88
Insurance/bond application denied	233/254	92
Social discrimination	201/250	80
Receiving placebo and not vaccine	166/254	65
Other concerns	24/88	27

\*Participants could cite more than one concern. The denominators for each item vary slightly because not all participants provided a response to each item.



doctors reporting this concern,  $P = 0.003$ ) and those in active clinical practice (with 73% of those in active practice versus 61% of those not in active practice citing this concern,  $P = 0.044$ ).

Overall, 39% of respondents ( $N = 113$ ) stated that they would not be willing to recruit patients, 24% (69) were uncertain about recruitment, and only 37% (107) were willing to recruit. Female doctors were less likely to be willing to recruit patients (22%, versus 44% for male doctors;  $P = 0.002$ ). Willingness to participate in vaccine trials was strongly associated with willingness to recruit patients into trials — 77% of doctors willing to participate in the trials themselves were also willing to recruit patients, while only 27% of doctors not willing to participate stated that they were prepared to recruit patients ( $P < 0.001$ ).

The final question of the survey asked again about subjects' willingness to participate in vaccine trials to evaluate whether the act of completing the questionnaire and thinking through trial-related concerns may change respondents' opinions. When respondents were asked again, willingness to participate in a vaccine trial decreased substantially to 11% of all respondents ( $N = 33$ ) stating their willingness (compared with 20% at the start of the survey).

## DISCUSSION

This study highlights the views on HIV vaccine trial participation among a sample of the medical profession in South Africa. There are a number of community education programmes underway to raise awareness of HIV vaccine trials and the potential for participation, including projects focused in rural KwaZulu-Natal<sup>6,7</sup> and Soweto<sup>8</sup> as well as a national campaign.<sup>9</sup> However, there are few data available on the willingness of various potential study populations to participate in vaccine trials, and there are no initiatives that target medical doctors in particular. As important 'gatekeepers' within many communities, the attitudes of health care workers are important determinants of local responses to HIV vaccines and the possibility of trial participation.

Our finding of a decrease in willingness to participate in HIV vaccine trials after being given additional information or time to consider the decision has been documented in a number of studies from France,<sup>10</sup> Thailand,<sup>11</sup> and the USA.<sup>4,12</sup> In addition, the concerns regarding HIV vaccines noted by the participants in this study parallel those expressed in similar studies from other settings.<sup>11-13</sup> The main concern regarding both doctors' own participation, and their perceptions of patients' willingness to participate, relate to potential of the vaccine to cause infection. Clearly this is a central issue that requires attention in existing community education initiatives, as well as detailed explanation in the recruitment and informed consent materials given to potential trial participants.

Perhaps the most surprising aspect of these results is related to the study population involved. Medical doctors are likely to possess a much better understanding of the role scientific research plays in improving health care, and we had anticipated that the levels of willingness to participate in HIV vaccine trials would be relatively high in this sample. The low levels of willingness documented here emphasise the importance of targeting HIV vaccine awareness materials at medical doctors and other health care professionals, and recognising more broadly that even relatively well-educated populations with substantial biomedical knowledge are likely to have major misconceptions about experimental HIV vaccines. As the search for an HIV vaccine continues, and South Africa moves closer to large-scale HIV vaccine trials, this study underscores the importance of continued, intensive preparatory work to overcome barriers to HIV vaccine trial participation in any population.

This study was funded by the Departments of Family Medicine and Virology at the University of Stellenbosch. The manuscript was prepared with support from the Fogarty AIDS Information, Training and Research Programme, Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA.

The authors thank Mr C J van Tonder, Mrs E Visagie and Mrs H Otto for their assistance in organising the postal survey and inputting data. Beryl Koblin provided valuable comments on earlier drafts of this manuscript. We are also grateful to all study participants for completing the questionnaires.

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Accepted 27 August 2002.