

Original research article

## The acceptability of an injectable, once-a-month male contraceptive in China

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### Abstract

**Purpose:** An acceptability study of an injectable preparation of the synthetic steroid testosterone undecanoate as a once-a-month male contraceptive method was carried out concurrently with, but independently from, a clinical safety and efficacy trial of this preparation in China, from 1997 to 1999.

**Method:** Three hundred eight men, the entire group of volunteers enrolled in the clinical trial, were interviewed using a structured questionnaire. In addition, 24 sessions of focus group discussions and 54 in-depth interviews were conducted with a broad range of stakeholders, including men enrolled in the trial and their wives, potential users, service providers, principal investigators of the six participating clinical trial centers, provincial and national policy makers, and experts engaged in research and development of male methods of contraception.

**Results:** Overall, men found the regimen to be acceptable, and most reported no change or an improvement in their well-being as a result of participating in the clinical study. The frequency of the injections, monthly semen analyses and the need to use another contraceptive method during the period of sperm suppression were reported inconveniences of the trial.

**Conclusion:** Further research is needed to assess the long-term safety, continuation rates, satisfaction among users and issues related to service delivery.

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### 1. Introduction

The development and introduction of a new fertility-regulating method into family planning programs would expand the choice and better meet the needs and preferences of users, particularly those who are dissatisfied with the range of methods currently available. As in other countries around the world, women in China are the predominant users of contraceptives. As recently as 2003, the use of available male methods remained fairly uncommon in China, with only 7.7% of men having had a vasectomy and 5.3% using condoms [1]. Increasing the availability and choice of contraceptives for men is likely to increase the chances that couples will find a contraceptive option that meets their particular needs and that more men will share in the

responsibility for contraception. In cases where a woman is unable to use a contraceptive and the man is unwilling to have a vasectomy or use a condom, a hormonal method for men may provide an appealing alternative.

From 1997 to 1999, a multicenter clinical trial to assess the safety and contraceptive efficacy of an injectable hormonal preparation, testosterone undecanoate (TU), in men was undertaken in six Chinese provinces (Hebei, Henan, Jiangsu, Sichuan, Shandong and Yunnan). According to the study protocol, during the first phase of the study (sperm suppression), an initial loading dose of 1000 mg TU was administered, followed by injections of 500 mg TU at monthly intervals. The men were followed until their sperm concentrations were suppressed to a level generally considered as compatible with contraception, or until they had received six monthly injections. At this time, partners of men whose sperm concentrations were adequately suppressed were asked to stop using any other contraceptive

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method, and the men continued to receive 500 mg TU at monthly intervals for the next 6 months. The results of the clinical trial have been published elsewhere [2]. An independent acceptability study was conducted in conjunction with the efficacy trial. The objective of this component of the study was to investigate the acceptability of the male injectable contraceptive method under study and to identify the sociocultural determinants of the attitudes and behaviors of study participants regarding the method. In addition, the views of a variety of stakeholders were sought with regard to the acceptability and feasibility of an injectable male contraceptive.

## 2. Data and methods

The acceptability study was independent of the clinical trial both in terms of its implementation and the investigators' responsibilities. Quantitative data were collected using a structured questionnaire from all 308 subjects who accepted the TU injectable contraceptive method, as well as from their wives. The subjects were interviewed at the first medical consultation following recruitment into the study, at the fourth and eighth months after accepting the first injection, and at the time the subjects withdrew from the clinical trial or after they received the final injection, prior to recovery. Wives of the subjects were interviewed at the fourth and eighth months after the first injection. Interviews were conducted after receiving the informed consent, which was provided by all participants in the trial.

Qualitative data were collected using focus group discussions (FGDs) and in-depth interviews. Participants for FGDs and in-depth interviews were selected randomly from the list of the subjects participating in the clinical trial. The wives of those selected subjects also participated in FGDs and in-depth interviews. Male and female contraceptive users who were not participating in the clinical trial were selected for FGDs and in-depth interviews from available lists of married women of reproductive age registered at the family planning office. The participants were informed of the study purpose and procedures, including confidentiality and privacy, before being asked for their informed consent to take part in FGDs and/or in-depth interviews. The sites for the conduct of FGDs were chosen to be different from clinics and convenient for participants. The FGDs and in-depth interviews were held in school classrooms, factory meeting rooms or the offices of local leaders. The rooms for FGDs were relatively private and comfortable. Focus group discussions with husbands and wives were conducted separately.

Twenty-four FGD sessions were organized; six of the sessions included a total of 49 subjects (each session included eight to nine participants) who were using the male injectable method. Six sessions included 45 wives of the subjects (each session included seven to nine participants) who were using the injectable method. Six sessions included 34 men (each session included five to eight

participants) who either had a vasectomy or were using the condom, and six sessions included 34 men (each session including five to eight participants) whose wives were using methods but they were not.

Fifty-four in-depth interviews were also conducted. Among the subjects in the trial, six were interviewed in-depth within the injection period and 12 were interviewed 6 weeks after receiving the last injection (including six men who expressed a willingness to use the method again and six men who were unwilling to use TU again). Ten men who withdrew from the clinical trial (2 out of the 12 men who discontinued moved to other provinces and could not be located), and two subjects whose sperm concentrations were not sufficiently suppressed after receiving injections of TU for the initial 6 months were also interviewed. In-depth interviews were also conducted with eight providers who administered injections to male participants and eight policy makers (six from the provincial level and two from the national level family planning program). The six principal investigators in charge of the clinical trial in the various study centers were also interviewed. Finally, two andrologists with extensive experience in research on male contraceptive method development were interviewed.

## 3. Results

The majority of all men who enrolled into the clinical trial (67%), and over half of their wives, had completed secondary or higher education. Over three-fourths of all men and their wives worked in agriculture and lived in rural areas. The majority of the subjects were between the ages of 25 and 34 years, and about half of them had one living child. The mean age of wives was 29 years, the mean duration of their first marriage was 8 years, and about 65% of wives had their own income.

### 3.1. Motivation, decision making and communication regarding participation in clinical trial

Results from the qualitative and quantitative data suggest that men had various reasons for participating in the clinical trial. The respondents were asked to indicate which reasons, from a given list, best applied to their situation. Table 1 indicates the reported level of importance of various reasons for joining the trial. Around 90% of the subjects reported "sharing responsibility for contraception," "contributing to solving the population problem" and "doing a good thing for my country" as somewhat very important reasons for joining the trial. It is difficult to determine the extent to which these are socially desirable responses. Financial compensation was not an important reason for the majority of the subjects (59%) to join the trial. Note that a modest amount of financial compensation was provided to cover transportation and the inconvenience of blood tests and semen analyses.

Men decided to enroll in the trial voluntarily and signed an informed consent form prior to participating in the study. Some participants joined the clinical trial because their

Table 1  
Distribution of subjects by reported reasons for joining the clinical trial

| Statement   | Level of importance (%) |                |                    |               | Total |
|---|-------------------------|----------------|--------------------|---------------|-------|
|   | Number                  | Very important | Somewhat important | Not important |       |
| I like to be involved in new things                         | 308                     | 25.0           | 56.8               | 18.2          | 100.0 |
| I felt proud in contributing to scientific advancement      | 308                     | 26.9           | 51.6               | 21.4          | 100.0 |
| I felt I was a pioneer of a new method of contraception     | 308                     | 24.4           | 46.1               | 29.5          | 100.0 |
| I believe men should share responsibility for contraception | 308                     | 41.2           | 51.0               | 7.8           | 100.0 |
| My wife wanted me to take responsibility for contraception  | 308                     | 23.1           | 44.8               | 32.1          | 100.0 |
| I felt I was doing a good thing for my country              | 308                     | 36.7           | 52.9               | 7.9           | 100.0 |
| I joined the trial for financial compensation               | 308                     | 12.7           | 28.6               | 58.8          | 100.0 |
| I felt I was contributing to solving the population problem | 308                     | 41.6           | 48.7               | 9.7           | 100.0 |

wives had problems in using the IUD or in using other female contraceptive methods (Table 1).

This trial is ‘unprecedented.’ Nobody knows if it [TU] is good or not good because nobody used it before. There should be somebody to use it for the first time. I’ll be one of the participants to support this trial (Jiangsu — 34-year-old factory worker, female, one boy, married for 5 years, FGD).

Table 2 provides information regarding the decision making, timing and people with whom the subjects discussed their participation in the trial. Although 30% of the subjects discussed with friends, relatives (other than their wives) or colleagues about their participation in the trial before deciding to join, 13% informed their friends after the enrollment and over half (57%) did not inform anyone. Participation in contraceptive trials still remains a sensitive matter, especially among men, and for this reason, many men did not disclose this information to others.

In the in-depth interviews, one subject reported that he did not want others to know that he had joined the clinical trial because he was afraid that his friends would think “he is silly to take the risk.” One subject reported that he did not discuss joining the trial with other men, as he thought that they would mock him and say that he was “afraid of his wife.” About 59% of men who were involved in the clinical trial stated that they were encouraged by their wives to join the study, whereas 35% of men answered, “My wife left the decision up to me” (Table 2). Very few wives opposed their husbands’ participation in the trial (2.3%), and about 4% of the subjects did not inform their wives until after they were enrolled in the study.

Discussing contraception with friends in public is uncommon in China, especially in the rural areas. For example, one subject mentioned that peasants had no time to communicate on contraceptive methods with each other because they are more concerned about work-related activities.

Chinese, especially Chinese men, are so conservative that a man should be a man of gigantic stature, he can do something for his wife only at home, it does not matter, even you scold him. But outside home, his wife should keep his face and others should not know his use of a male method (Jiangsu — 31-year-old factory worker, female, one boy, married for 5 years, in-depth interview).

In one FGD, the wife of a subject said that she lied to her colleagues about taking part in the discussion because she did not want her colleagues to know that her husband had joined the trial on a male injectable contraceptive method. She told her colleagues instead that she had gone to see a doctor:

To tell you the truth, I told my colleagues that I’ll see a doctor instead of attending a (FGD) meeting (Jiangsu — 34-year-old factory worker, female, one boy, married for 5 years, FGD).

### 3.2. The physical and behavioral changes experienced during the study and the reported side effects

Previous research suggests that experiencing side effects with the use of a contraceptive method, regardless of clinical significance, is an important determinant of the method’s overall acceptability [3]. At months 4 and 8 of the clinical trial, interviewers asked the subjects an open-ended question about their feelings regarding the injections. Interviewers then recorded up to three of the subjects’ spontaneous responses verbatim. Relatively few subjects reportedly provided second and third reactions to the injection (36 and 6 subjects, respectively). Infrequent second and third responses could result from the interviewer’s failure to probe adequately as well as the real absence of additional reactions. The percentage distribution of all the first responses provided at months 4 and 8 of the clinical trial was reviewed for those who were interviewed on both occasions.

Table 2  
Influence of wife on the decision to join in the trial and communication with others about participation in the trial, total sample ( $n=308$ )

|  | %     |
|--|-------|
| <i>Decision making</i>   |       |
| My wife encouraged me to join in the study   | 58.8  |
| My wife left the decision up to me   | 34.7  |
| My wife did not want me to join in the study   | 2.3   |
| My wife did not know until after I had joined in the study                             | 4.2   |
| Total  | 100.0 |
| <i>Communication with friends, relatives and colleagues about joining in the trial</i> |       |
| Informed before deciding to join   | 30.2  |
| Informed after the enrollment  | 13.0  |
| Did not inform or discuss  | 56.8  |
| Total  | 100.0 |

About half of the respondents reported “no change/ nothing special” in response to this question at months 4 and 8 (53% and 48%, respectively). About 21% of the subjects reported that they “felt better” after the injection. Some subjects did spontaneously mention either an increase or a decrease in libido, energy and appetite at both interviews; however, there appears to be some tendency to report “increases” in physical attributes such as in libido, energy, strength, appetite, hair growth and body weight rather than a “decrease” in these at month 8 (12.7% vs. 2.1%).

In FGDs, most participants reported that the male injectable method had few side effects, including no obvious change in sexual life or sleep pattern. However, some in-depth interview respondents and FGD participants did report physical and behavioral changes over the course of the trial. Some reported that they could not sleep as well as before the trial, and some reported having acne or “papules” or that their skin became oilier. One principal investigator said, “About one third of subjects reported acne, most appearing on the face.”

As for the libido, it is so-so. Higher sex desire during the first 2 days; afterwards, the same as usual (Jiangsu — 37-year-old factory worker, male, one girl, married for 10 years, FGD).

A majority (about 60%) of FGD participants reported that their feelings of physical power, sexual interest, appetite or weight increased. However, a few reported that their physical power, interest in sex and satisfaction with sex declined, and yet, others reported that their testicles became “small and soft.”

### 3.3. Attitude toward male injectable contraceptive

Table 3 shows the percentage distribution of reasons for dissatisfaction with the method, by month of interview, among those who reported method inconvenience or dissatisfaction at month 4 or 8. Among men still enrolled in the trial, 27.4% (83 out of 303) perceived inconvenience at month 4 and 40.3% at month 8 (117 out of 290). It is thus

Table 3  
Perceived inconvenience and dissatisfaction of the method among men interviewed at months 4 and 8

| Reported reasons                           | At month 4 (%) | At month 8 (%) |
|--|----------------|----------------|
| Reasons for perceived inconvenience        | (n=83)         | (n=117)        |
| Have to come to clinic                     | 21.7           | 9.4            |
| Once a month is too frequent               | 72.3           | 76.9           |
| Have to wait at the clinic for a long time | 1.2            | 5.1            |
| Other reasons                              | 4.8            | 8.5            |
| Total                                      | 100.0          | 100.0          |
| Reasons for dissatisfaction                | (n=91)         | (n=117)        |
| Side effect                                | 12.1           | 6.0            |
| Inconvenience                              | 52.7           | 48.7           |
| Injection pain                             | 20.9           | 12.0           |
| Others                                     | 14.3           | 33.3           |
| Total                                      | 100.0          | 100.0          |

apparent that a majority of men did not report any inconvenience with the use of the method.

More than 72.3% of the subjects reporting method inconvenience stated that once-a-month administration was too frequent, whereas only 21.7% reported visiting the clinic as the main inconvenience of the method. Among the subjects who were dissatisfied with the method, 52.7% reported that they were dissatisfied because of the inconvenience of coming to the clinic every month, whereas 20.9% reported injection pain as the main reason for dissatisfaction at 4 months, and these percentage decreased to 48.7% and 12.0% at 8 months, respectively (see Table 3).

Most FGD participants considered the method to be “inconvenient,” although they also said that the method was simple and reversible. Having to use another contraceptive method during the initial sperm suppression phase, having to do sperm tests and having to do blood tests were reasons for the inconvenience of the method. Having to come to the clinic to receive this method was also seen as inconvenient by some FGD participants, but not by others:

Semen analysis once a month is indeed troublesome, we are peasants, we have to go out to make money, we have no time (Sichuan — 26-year-old male, farmer, one girl, married for 2 years, in-depth interview).

A few policy makers at the provincial level were opposed to introducing and promoting the male hormonal method in their province because of their perception that the method may influence family happiness (sexual life) or cause other social problems (such as rape, paid sex and extramarital pregnancy). They also suggested that the introduction of this method would increase the workload of providers and family planning workers and were worried about the costs for introducing the method to the local government.

This method increases the workload for providers and managers of family planning. In rural areas, especially, local family planning workers hope to promote long-acting, lower cost, simple to deliver and more effective methods (Jiangsu — provincial family planning policy maker, female, in-depth interview).

Nearly all participants, whether the subjects, the subjects’ wives, providers, experts or policy makers, mentioned that if the new hormonal method was proven to be safe and effective, it could be good news for women who do not want to or cannot use a female method. This would offer relief for some women who suffer from side effects of available female contraceptive methods. However, they were uncertain about the prospect of a wide uptake. Many expressed the need for further research on the long-term safety of the method. A few expressed their doubts about the safety of this method.

There are still some problems in introducing this method. First, frequency is not convenient for users; second, if costs are more than 10 Yuan monthly, it is not affordable for an average family; third, long-term safety is not

known and that is very important to the acceptability and introduction (Sichuan — provincial family planning policy maker, male, in-depth interview).

#### 4. Discussion and recommendations

The life-table analysis of data of the sperm suppression phase shows that about 95% of the clinical trial subjects were eligible to and chose to enter the efficacy phase of the study. No serious adverse life-threatening event occurred during the study [3]. Were the injectable to have a shorter suppression phase, longer injection interval, proven long-term safety and be more convenient, it would likely be acceptable to even more users. A safe, effective, convenient and affordable male contraceptive method is what most respondents preferred in study areas of China.

The evidence from this study showed that in China, women are likely to support their husbands using a male injectable method. Users have positive perspectives for this method, whereas nonusers have negative perspectives. Providers are likely to favor long-acting contraceptive methods over a monthly injectable, which would increase their workload. Policy makers maintain that they support additional research but are apprehensive about the introduction of the method into the family planning program in the light of the available evidence. A phase III trial of the same method is currently being conducted in China, and the results of the trial will provide more information about this method from a larger number of couples.

A number of factors influence the acceptance of the once-a-month injectable TU as a male contraceptive in China. First, a population's previous experience of contraceptive use influences the acceptability of new methods [4]. In China, the IUD is the predominant method, and it provides protection to users for many years. Couples experiencing no problem with the use of IUDs or another female contraceptive method may not wish to switch to a male contraceptive method. From the discussion with the principal investigators in the study centers, it is known that the process of recruiting participants for the clinic trial was difficult, and finally, they focused on couples who had problems with IUD use but did not want to get sterilized. According to the data collected in the present study, local family planning policy makers and providers are keen to promote and provide methods that are long acting, easy to provide and require less work. Men whose wives have had problems using the IUD or other female contraceptive methods, or whose wives do intend to have sterilization (according to the local regulations) after having had their second birth, may be more likely to participate in the clinical trial on the male injectable and eventually use this method if it becomes available. In the FGDs with wives who were asked why they supported their husbands to join this trial, most of them (70%) said that they had problems with using female contraceptive methods; otherwise, they

would use a female method rather than having their husband use male methods.

Second, side effects are a major concern for this male method. Although some short-term side effects, such as acne, may be tolerable to some subjects and the injection pain in the buttock may also be endured by some men, few (12 out of 308) subjects withdrew from the trial because of the concern or experience of side effects. Overall, most of the men in the trial (about 90%) expressed a concern about long-term safety and about recovery of fertility after discontinuation of use. The satisfaction and continuation rates with a longer period of use need to be evaluated.

Inconvenience was given as a main reason for dissatisfaction with the method. "Once-a-month" was too frequent for many subjects and is not convenient during the busy farming season or for people who travel for work. In some centers, the subjects made appointments with the township family planning clinics to have the injections. In other centers, providers went to the subjects' homes to give the injections. Increasing the length of the injection interval would be more convenient for providers and users and may promote the method's wider use when it becomes available. It should be noted that the blood and semen analyses, although important aspects of the clinical trial, would not be required in a marketed method of male contraception, with, perhaps, the exception of a semen analysis to verify sperm suppression after a certain period of use.

Overall, male contraception is a novelty in China. There are social pressures against its wider adoption in addition to the limited choices currently available. In China, talking about the contraceptive issue in public is still a sensitive matter, especially using male methods. For this reason, many couples did not disclose the information about their participation in the trial to others. People considered it embarrassing for a man to accept a contraceptive method. Some providers anticipated social problems (such as visiting prostitutes and extramarital sexuality activity) arising out of men's use of contraceptive methods. Finally, the perception that male contraceptive methods can influence sexual activity and consequently influence family happiness also persists in some areas; for example, one provider indicated that a woman may get pregnant even if her husband uses a contraceptive method; however, she would not become pregnant if she uses an effective female contraceptive method, such as the IUD.

The results of this study suggest a number of areas for further research. Studies should be undertaken to assess the long-term safety and efficacy of TU. As mentioned above, a phase III trial is ongoing in China. The effectiveness data obtained from a clinical trial might be quite different from what may emerge from a representative population-based samples of users. Policy makers in China would also like to know whether or not men can use this method safely over the long term. Assessments of continuation rates, method switching, use effectiveness and service-related needs under "natural" conditions are needed. Studies to extend the

injection interval and to develop a simple method to check sperm count would help to assess the effects of changes in these variables on method acceptability. Studies to investigate the potentially antagonist effects on TU of other hormonal medications such as prednisone should also be undertaken. Overall, this experimental male hormonal method potentially provides a choice to some couples, but its wider acceptability to users, and especially to nonusers and providers, remains to be established. The method used in the trial is as yet not available. The features of the male method that may eventually become available could differ from the one studied.

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