

# The need for a clinical trials research methodology training programme in Hong Kong

WF Lui, J Karlberg

Training courses in the concepts of clinical trials research methodology that include rules in good clinical practice have not yet been extensively implemented in Hong Kong. This study aims to define the current knowledge of rules in good clinical practice and identify any need for such training programmes. Between May and August 1996, 161 clinical research staff were asked non-randomly to fill in a questionnaire about their knowledge of research methodology and their interest in specific courses. The median number of correctly answered questions (maximum score, 20) was 5 and the mode was 4, which was the expected score if questions had been answered randomly. Only minor differences in score were detected between doctors, research staff, and industry employees. Many researchers were keen, however, to further their knowledge by attending future courses; on average, each person showed an interest in three of the eight proposed courses. The study shows that the knowledge of rules in good clinical practice among clinical research staff in Hong Kong is poor, but there is nevertheless a demand for training programmes.

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## Introduction

### *Concepts of good clinical practice*

Good clinical practice (GCP) is "a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials".<sup>1</sup> It was developed in response to some serious cases of fraud and abuse of patients' rights.<sup>2</sup> Since GCP rules were first made mandatory by the United States (US) Food and Drug Administration, they have been widely implemented by regulatory authorities in other countries, such as those in the European Union, Japan, Australia, and the member states of the World Health Organization.<sup>3</sup>

A guideline for GCP from the recent International Conference on Harmonization of GCP is now accepted as a unified standard by regulatory authorities and pharmaceutical companies in the US, European Union, and Japan.<sup>1</sup> This guideline creates a general scientific bench-mark for clinical trials research methodology. The aims of the guideline are to protect study subjects,

and to improve the ethical and scientific qualities of studies. A higher quality of research ensures the safety of study subjects and the development of better medical care and products for patients who are in need of new therapy. Rules for GCP also provide "a resource for editors to determine the acceptability of reported research for publication".<sup>4</sup>

### *Evidence-based medicine*

Evidence-based medicine "de-emphasises intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research".<sup>5</sup> In other words, decision making in clinical practice must be based on research-generated scientific evidence. The strength of such evidence, however, depends on the ways in which it has been obtained. One assignment of the Canadian Task Force on the Periodic Health Examination was to develop a set of criteria for evaluating scientific evidence on the effectiveness of any preventive intervention.<sup>6</sup> These criteria were reviewed by the US Preventive Services Task Force which classified the quality of evidence according to the way it was collected. Evidence was classed as grade I if it came from at least one properly randomised controlled trial; grade II if it came from controlled trials without randomisation, designed cohort or case-

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Clinical Trials Centre, Department of Paediatrics, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong  
WF Lui, BN, RN  
J Karlberg, MD, PhD

Correspondence to: Ms WF Lui

control analytic studies, or uncontrolled experiments; and grade III if from clinical experience or descriptive studies.<sup>6</sup> A properly designed randomised clinical trial is the most valid study and when performed properly, it provides the strongest evidence on which to make a clinical decision. The medical practice from this decision will be more beneficial and favourable.

### ***The need for training***

Many investigators and their research staff or associates are not fully educated about the principles and practical application of GCP rules.<sup>7</sup> Gennery<sup>8</sup> stated that training is one of the most critical areas in the process of GCP. Training in clinical trials research methodology that is based on GCP rules should be mandatory for all investigators and their clinical research staff. It is also important for medical students, residents, fellows, physicians, graduate students in health or other related disciplines, and personnel from the pharmaceutical industry and regulatory authorities.<sup>9</sup> Training in GCP teaches these scientists how to improve the standard of clinical trials research.

Productivity is, in part, a function of training and experience<sup>10,11</sup> and can be increased by structured training in research methodology.<sup>12</sup> Developing well-trained and experienced research staff is vital to the success of any study. Clinical research training is not usually emphasised for clinical research faculty members,<sup>13</sup> however, and they may even be "often deprived of valuable training in research methodology".<sup>14</sup>

### ***Clinical trials research methodology training programmes***

In many institutions, there are formal and informal training programmes in clinical trials research methodology, and GCP rules for clinical research staff or associates.<sup>9,15</sup> These include academic programmes, training by professional societies, commercial training programmes, and company training programmes.<sup>16</sup> Academic institutions such as the University of North Carolina, University of Michigan, and Temple University in the US, and the University of Montreal in Canada, offer some higher-degree courses in clinical research methodology.<sup>9</sup> Professional societies, including the US Food and Drug Administration, the American Academy of Allergy and Immunology, and the Associates of Clinical Pharmacology, sponsor training programmes for clinical research staff. The University of Indonesia runs workshops on GCP for clinicians and industry representatives.<sup>16</sup> There are also some university-affiliated postgraduate fellowship and residency programmes.<sup>17</sup>

A clinical trials research training programme should include research studies and the teaching of current international GCP standards, and basic approaches to and methodology of clinical trials. A syllabus for a training course on clinical trial research methods has been described by Spilker,<sup>9</sup> and contents of suitable curricula have been proposed.<sup>9,14</sup>

### ***Study objectives***

In Hong Kong, the training of research staff in the concepts of clinical trials research methodology has not yet been extensively implemented. The aims of this study were to define the current knowledge of GCP rules and clinical trials research methodology, and to identify any need for a clinical trials research methodology training programme for various levels of clinical research staff in Hong Kong.

### ***Materials and methods***

A non-random sample of 161 people was asked between May and August 1996 to answer a standardised questionnaire. Doctors and clinical research staff participating at the study were those attending various workshops or lectures at the Queen Mary and Pamela Youde Nethersole Eastern hospitals. The study objectives were also described in a letter which was mailed to 30 pharmaceutical companies in Hong Kong and an appointment was made if a company agreed to participate. Eighty-three (51.6%) participants were doctors and 26 (16.1%) were clinical research staff or research associates, most of whom worked at the Queen Mary Hospital. Another 52 (32.3%) participants were employees from the pharmaceutical industry in Hong Kong.

The questionnaire consisted of two parts. The first contained 20 multiple-choice questions on clinical trials research methodology. There were five choices but only one correct answer for each question. Most questions concerning GCP rules were based on the 1990 European GCP guidelines. Questions tested knowledge in the following areas: basic concepts of GCP, roles and responsibilities of parties, ethics, data management, biostatistics, and basic concepts of clinical trials. In the second part of the questionnaire, subjects were asked about their willingness to participate in eight specific courses related to clinical trials research methodology (yes/no answers). These courses were about GCP knowledge, information searching, scientific report writing, study protocol, biostatistics, computer programmes, quality of life estimates, and laboratory testing. The list was based on Spilker's list of specific clinical research topics.<sup>9</sup> Preferences for

**Percentages of questionnaire respondents answering correctly**

Question	Respondents, n=161 No. (%)
When was the GCP guideline valid in Europe?	29 (18.0)
Which countries practise the GCP guideline?	15 (9.3)
What are the main objectives of the GCP guideline?	38 (23.6)
What is the meaning of a phase II trial?	25 (15.5)
Who can be a principal investigator?	36 (22.4)
Who should review the study budget?	82 (50.9)
What is the minimum number of members on an Ethics Committee?	43 (26.7)
Which document is not required to be submitted to an Ethics Committee?	20 (12.4)
What kind of persons can be recruited in a clinical study?	58 (36.0)
What information must be supplied to the subject?	85 (52.8)
Who can be an independent witness?	65 (40.4)
What is the characteristic of an experimental study?	89 (55.3)
How should a stratified block randomisation be performed?	52 (32.3)
What are the reasons for undertaking sample size calculation?	70 (43.5)
What are needed for sample size calculation?	65 (40.4)
What are the roles of a biostatistician in a clinical study?	32 (19.9)
What information should be included in a protocol?	17 (10.6)
How should principal investigators make corrections in a case report form?	41 (25.5)
What are the sources of an adverse event?	37 (23.0)
How long should a principal investigator keep study documents?	27 (16.8)

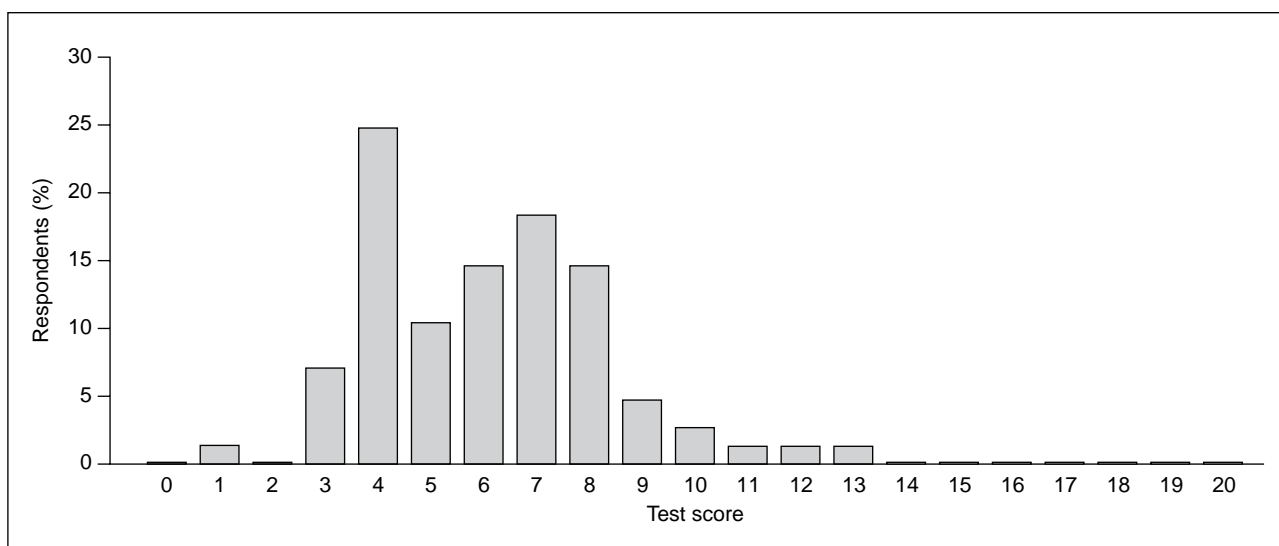
duration of participation in the various programmes (full time, part time, day time, evening, weekday, or weekend) were also assessed.

A pilot study based on eight clinical research staff was performed to ensure the comprehensibility and completeness of the questionnaire, and modifications were made accordingly. A simple statistical description of the findings was made using the *Statistical Analysis System* for Windows, Release 6.08.<sup>18</sup>

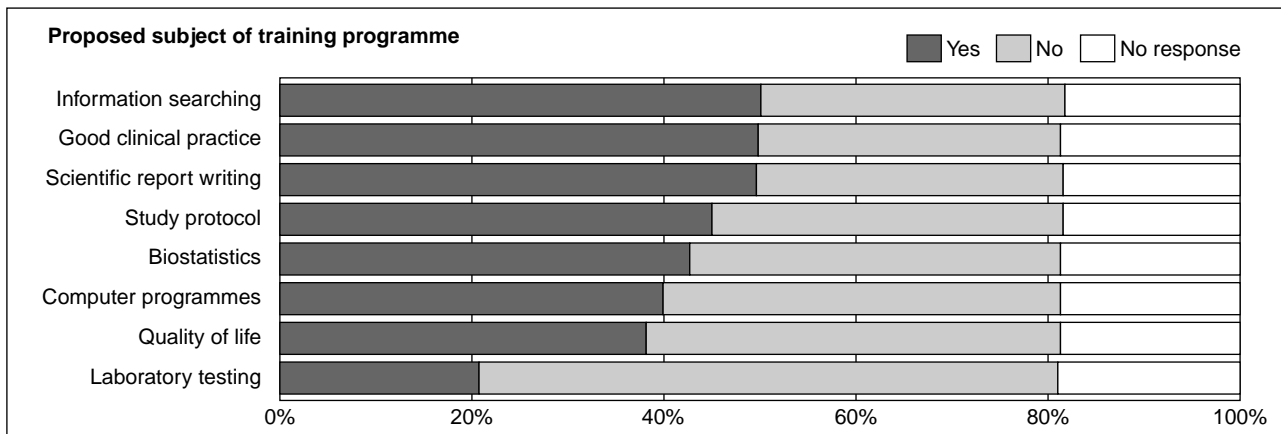
## Results

### *Current knowledge of clinical trials research methodology*

The Box shows the percentages of correct answers scored in response to the 20 questions. The question in which the highest score was achieved was about the characteristics of an experimental study (55.3% correct). The lowest score was about countries which practise GCP rules (9.3% correct).



**Fig 1. Frequency distribution of the total score of correct answers**



**Fig 2. Bar chart showing respondents' interest in various training programmes**

Figure 1 depicts the frequency distribution of the total score of correct answers among the 161 study subjects. The median score of correctly answered multiple-choice questions was 5 (25%) for the whole study group. The mode was 4 (20%) which was the score expected if answers were only random guesses. Only minor differences were detected in median correct answers between the three working groups (range of scores, 5-6). The median number of correct answers was 6.0 for doctors, 5.5 for research staff, and 5.0 for industry employees.

**Preferences for participation in the training programmes**

Figure 2 shows the percentages of people who expressed interest in various training programmes. The most popular courses were information searching, GCP, and scientific report writing; the least popular was laboratory testing.

**Comparison between the three working groups**

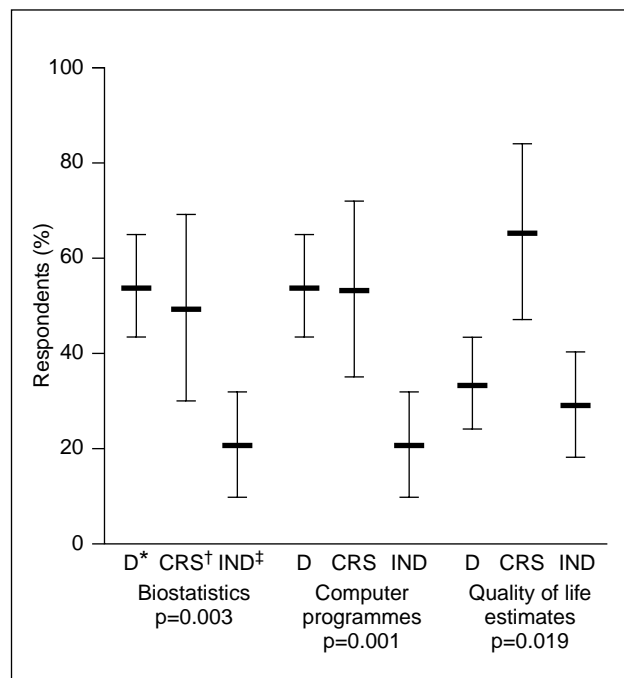
Figure 3 depicts the interest among the three working groups (doctors, clinical research staff, and pharmaceutical industry employees) in participating in the various training programmes. There were significant differences ( $P < 0.05$ ,  $\chi^2$  test) between the three groups for courses related to biostatistics, computer programmes, and quality of life estimates.

**Discussion**

This study found that there was little knowledge of GCP rules and clinical trials research methodology among research staff, and that there is a need for the introduction of a training programme in clinical trials research methodology for research staff in Hong Kong. The study may be criticised on the grounds of not using a randomised sampling technique. The questions asked in the questionnaire may also not be the best

way to assess the current knowledge of clinical trials research methodology. The results, however, demonstrate researchers' poor knowledge of clinical trials research methodology, particularly since the most frequent score was that expected if answers had been randomly chosen.

The study also found minor differences among the three professional groups, namely doctors, research staff, and industry employees. This may reflect differences in levels of education in research methodology; for example, the most traditional method of training is



\*D doctors  
 †CRS clinical research staff  
 ‡IND pharmaceutical industry employees

**Fig 3. Differences in professional groups' interest in various training programmes**

The Chi squared test was used;  $P > 0.05$  for the courses not named above; results are expressed as mean  $\pm$  SD

by coaching—a method that may be limited due to workload constraints and lack of qualified mentors. Since clinical research of different disciplines has much in common, it would be appropriate to build up a systematic training programme to address the individual needs of both experienced and inexperienced research staff. The training programme should begin before participation of the researcher in a clinical study, and should continue throughout that study. All people involved in clinical trials, particularly those who have direct contact with subjects, need to understand fully their responsibilities as defined by rules of GCP. They should understand how to obtain informed consent correctly, complete case record forms accurately, and monitor and record any adverse events properly. This should result in improved staff performance which will increase the safety of the study subjects and contribute to quality data.

This study identified a strong demand for training programmes related to clinical trials research methodology. On average, each person expressed an interest in participating in at least three of the eight courses listed. Training programmes such as workshops on the GCP guideline have been held elsewhere in Asia, for example, Singapore, Indonesia, Malaysia, Thailand, and the Philippines, and recently in Hong Kong.<sup>16</sup>

Since 1990, many reports on the ethnic differences between the Chinese and Caucasian races have been published. They show there is limited mutual acceptance of data from trials carried out in different ethnic populations.<sup>19,20</sup> For example, there are differences between approved dosages of antihypertensives, antiarrhythmics, antibiotics, antibacterials, antivirals, antihistamines, and psychotropics, as used in Japan and in western countries.<sup>21</sup> Instead of accepting data on other ethnic groups, Hong Kong studies would provide better, more accurate information on the most suitable regimens and possible side effects for Asian populations. Ultimately, performing more studies of high quality will improve the availability of important, new, and better medical care and products to patients.

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