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Development and validation of the Chinese oral anticoagulants knowledge tool (C-OAKT): A pilot study

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A R T I C L E I N F O

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A B S T R A C T

Objective: To develop and validate an oral anticoagulant knowledge tool for Chinese-speaking patients treated with warfarin or direct oral anticoagulants (DOACs) in Hong Kong.

Method: This pilot validation study consisted of the following three phases: (1) the development of a knowledge tool and content validity assessment; (2) a pilot study of 200 participants, consisting of 100 patients taking warfarin or DOACs, 50 pharmacists, and 50 members of the general public; and (3) known-group validity and reliability assessments.

Results: A 19-item "Chinese Oral Anticoagulants Knowledge Tool (C-OAKT)" was developed with a scale content validity index of 0.95. The mean score for known-group validity was significantly higher in the pharmacist group than the patient groups, and the patient groups scored significantly higher than the general public (mean ± standard deviation [SD] = 90.00 ± 7.11 vs. 51.55 ± 17.49 vs. 19.0 ± 15.42, respectively; $p < 0.001$). The mean score was higher for patients who attended a pharmacist-managed anticoagulant therapy management clinic (PAC) than for non-PAC patients (mean ± SD = 56.80 ± 13.60 vs. 46.30 ± 9.43; $p = 0.004$). An analysis of internal consistency showed a Cronbach's alpha value of 0.86.

Conclusion: The results of the pilot validation study suggested that the C-OAKT is a valid and reliable instrument for assessing patients' knowledge of oral anticoagulants in ambulatory care settings.

Innovations: This is the first validated Chinese version of an anticoagulant knowledge assessment tool. This tool will be utilized in public hospitals in Hong Kong, and will facilitate future research exploring the relationship between anticoagulant knowledge and patient-related outcomes.

1. Introduction

Warfarin and direct oral anticoagulants (DOACs) are commonly prescribed for the treatment and prevention of thromboembolic events [1]. Warfarin is characterized by a low therapeutic index and interindividual treatment response variability, with fluctuations in the dose–response relationship. It has been implicated in adverse drug events due to many factors, such as the complexity of dosing and monitoring, and numerous drug–drug and drug–food interactions [2]. DOACs, also known as non-vitamin-K oral anticoagulants, are a newer class of anticoagulants with a more favorable toxicity profile. They do not require routine monitoring, they have a fixed-dose regimen, and they have no restrictions on the dietary consumption of vitamin-K-containing food. DOACs have been found to be similarly effective to warfarin at preventing thromboembolic events in some health conditions [3-6]. The greater convenience of DOACs over warfarin has led to an increase in the

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prescribing of DOACs to prevent thromboembolic events.

Despite the increasing popularity of DOACs, their use is associated with drug-related problems [7], such as inappropriate dosing and drug–drug interactions. The dosing of DOACs is affected by the indication, treatment duration, renal function, patient weight, and concomitant medications. For example, older patients taking DOACs are susceptible to an increased risk of bleeding due to decreased drug metabolism and hepatic and renal dysfunction [7]. Patients who require long-term treatment with DOACs may also have problems with adherence. Therefore, educating patients on the importance of DOACs and recognizing the signs and symptoms of bleeding is important to ensure that they know how to seek appropriate help in a timely manner [8].

Health literacy is a major contributing factor to the adequate self-management of anticoagulation treatment and the reduction in the frequency of complications. Patients' knowledge of anticoagulants may affect their treatment outcomes, thus preventing the occurrence of and promoting the early recognition of bleeding events [9]. One study evaluated the association between anticoagulation knowledge and treatment outcomes in 323 older patients taking warfarin, and compared the rate of bleeding events and the quality of anticoagulation across various socioeconomic and clinical variables [10]. That study found that inadequate anticoagulation knowledge was the major factor predicting bleeding complications [10]. Another study conducted in Hong Kong by Tang et al. found a positive correlation between patients' knowledge of warfarin and the number of international normalized ratio (INR) values within the target range [11]. A Vietnamese study also demonstrated a strong association between patients' knowledge and treatment adherence in patients taking DOACs [12]. The findings from these studies suggest that an adequate knowledge of anticoagulants may lead to better clinical outcomes and may reduce the risk of adverse events.

Several studies have attempted to develop validated scales to assess patients' anticoagulant knowledge [13-16]. Currently, only two warfarin knowledge tools, the Anticoagulant Knowledge Assessment (AKA) developed by Briggs et al. [13] and the Oral Anticoagulant Knowledge Test (OAK) developed by Zeolla et al. [14], have established content and construct validity (Table 1). However, both of these knowledge tools were designed to assess knowledge regarding warfarin only, and they are not applicable to DOACs. Although the English version of the AKA was translated into a Chinese version, which was used to assess patients' warfarin knowledge and anticoagulation control in mainland China, little is known about its psychometric and measurement properties [15]. There is only one existing knowledge tool, the Anticoagulant Knowledge Tool (AKT) developed by Obamiro et al. [16], that has been developed and validated for both warfarin and DOACs. However, some items may not be relevant in Hong Kong due to cultural differences. For example, patients are required to give their latest INR value in the AKT. However, most patients in Hong Kong who are treated in a public hospital are not told their exact INR value, as their INR values are typically monitored by healthcare professionals, and they are only informed of the targeted range and whether they are above or below the target. Therefore, it would be difficult for patients in Hong Kong to answer this question correctly. In the absence of a valid and reliable instrument, clinicians cannot accurately and objectively measure patients' knowledge, the impact of different disciplinary-managed anticoagulant clinics on patients' knowledge, or the correlation between patients' knowledge and anticoagulation control and outcomes.

In Hong Kong, the Hospital Authority is the sole public healthcare provider and it serves >90% of Hong Kong residents. According to the Clinical Data Analysis and Reporting System, an in-house repository managed by the Hospital Authority, there are currently 114,972 patients utilizing public healthcare services who were prescribed oral anticoagulants from 2018 to 2022. However, there is currently no standardized and validated tool to assess patients' knowledge of oral anticoagulants in an ambulatory care setting.

The objective of this pilot study was to develop and validate a Chinese oral anticoagulant knowledge tool that is applicable to all oral anticoagulants. As part of this pilot validation study, the tool was used to generate preliminary data to assess the impact of a pharmacist-led anticoagulation clinic (PAC) on patients' knowledge of warfarin and DOACs.

2. Methods

2.1. Study design

This prospective study was conducted at the outpatient clinics of the Queen Elizabeth Hospital (QEH) from January 2022 to March 2022. The QEH is a regional tertiary care public hospital that serves as one of the major hubs for providing care for patients with cardiovascular diseases in the Kowloon area of Hong Kong. This study was approved by the Research Ethics Committee of Kowloon Central/Kowloon East (Ref: KC/KE-21-0275/ER-3).

2.2. Study procedure

This pilot validation study consisted of the following three phases: (1) the development of a knowledge tool and content validity assessment, (2) a pilot study, and (3) known-group validity and reliability assessments of the newly developed tool.

2.2.1. Phase 1: Development of the Chinese oral anticoagulation knowledge tool (C-OAKT)

2.2.1.1. Designing the questionnaire. A review of patient educational materials and the health literacy of patients with cardiovascular and

Table 1
Comparison of the Existing Anticoagulant Knowledge Tools and the Newly Developed Chinese Oral Anticoagulant Knowledge Tool (C-OAKT).

	Oral Anticoagulation Knowledge test (OAK)	Anticoagulation Knowledge Tool (AKT)	Anticoagulant Knowledge Assessment (AKA)	Chinese Oral Anticoagulant Knowledge Tool (C-OAKT)
Reference	Zeolla et al.	Obamiro et al.	Briggs et al.	Chan et al.
Target patients	Patients on warfarin	Patients on warfarin and DOAC	Patients on warfarin	Patients on warfarin and DOAC
Construct validity tests	Comparison of scores between warfarin group and non-warfarin group	Comparison of scores among pharmacists, patients on OAC, and members of the public	Rasch analysis	Comparison of scores among pharmacists, patients on OAC and members of the public
Reliability tests	Test-retest reliability and internal consistency	test-retest reliability and internal consistency	Item separation index	Internal consistency
Number of items	20	20 items on warfarin 28 items on DOAC	29	14 items on warfarin 19 items on DOAC
Types of question	Multiple choice questions only	Open-ended and multiple choice questions	Multiple choice questions only	Open-ended, and multiple choice questions
Language(s) available	Multiple language versions (English, Turkish, Brazilian, etc.)	English and Italian	English	Chinese

DOAC: direct-acting oral anticoagulants; OAC: oral anticoagulants.

thromboembolic diseases was conducted, using both the general literature [17-20] and local practices [21-23]. The existing oral anticoagulant-knowledge-assessment tools (Table 1), namely the AKT [16], AKA [13], and OAK [14], were reviewed. The items from these knowledge-assessment tools were divided into five categories: basic drug information, adverse effects, drug–drug interactions, drug monitoring parameters, and dietary considerations. Some items that were irrelevant or inappropriate in Hong Kong were deleted or modified. For example, Warfarin-diet interactions were asked in the AKA with options including celery, carrots, cole slaw and green beans which were not the foods commonly consumed in Hong Kong [13]. Therefore, this question was modified to include foods that are commonly consumed by people in Hong Kong, such as amaranth, chives, green yard-long beans, kale, and spinach. Moreover, INR value monitoring interval was asked in OAK but the monitor interval varies between patients in Hong Kong who are treated in a public hospital [14]. Therefore, this question was modified to ask if routine INR tests are needed for patients treated on anticoagulant medicine. Patients are required to answer their latest INR value in the AKT [16]. However, it would be difficult for patients in Hong Kong to answer this question correctly as their INR values are typically monitored by healthcare professionals, and they are only informed of the targeted range and whether they are above or below the target. Therefore, this question was deleted.

Fifty open-ended or multiple-choice questions were developed based on common topics covered in the literature review, including basic drug information, adverse effects, drug–drug interactions, drug monitoring parameters, and dietary considerations. The relevance of each question to anticoagulation knowledge was then reviewed by four pharmacists who managed a PAC. The PAC pharmacists were registered pharmacists with ≥4 years of practice experience who had attained post-graduate clinical qualifications in internal medicine or ambulatory care and anticoagulation therapy management through accredited programs, such as the American Board of Medical Specialties certification or the Advanced Postgraduate Certificate Program of the Institute of Advanced Allied Health Studies.

The PAC pharmacists rated the questions on a scale of 1 to 5 (1 = strongly disagree, 5 = strongly agree). This ranking was used to eliminate irrelevant questions, and the process resulted in a preliminary scale of 19 items that consisted of both open-ended and multiple-choice questions.

2.2.1.2. Assessing content validity. Content validity refers to the extent to which a measure has an appropriate sample of items to represent the construct of interest [24]. The relevance of each item was assessed by a 10-member expert panel that included four PAC pharmacists and six physicians specializing in cardiology, neurology, or internal medicine. The items were sent to each member of the expert panel, and they rated each item independently on a 4-point ordinal scale (1 = not relevant, 2 = somewhat relevant, 3 = quite relevant, 4 = highly relevant) to assess the relevance of each item.

The content validity index for each item (I-CVI) and the overall content validity of the scale (S-CVI) were then calculated using the method of Polit et al. [25,26] (Supplement 1). The CVI is one of the most widely reported approaches for the quantitative evaluation of content validity in instrument development [27-29]. This approach is adopted in the development of the AKT assessment tool too [16]. The relevance of each item was determined based on the modified kappa index (k*) value. Accordingly, a k* value of 0.40–0.59 indicated fair content validity, a k* value of 0.60–0.74 indicated good content validity, and a k* value >0.74 indicated excellent content validity [30]. To ensure that the newly developed tool only included clinically relevant items, those items with a k* value <0.60 were excluded from the draft questionnaire.

2.2.2. Phase 2: Pilot study

A pilot study was performed on 20 participants to review the clarity and readability of the questionnaire. A paper version of the questionnaire was distributed to five patients treated with warfarin, five patients treated with DOAC, five pharmacists, and five members of the general public. After the participants had completed the questionnaire, a short interview was conducted by the investigators to identify any problematic or culturally offensive terms in the draft questionnaires. After completion of the pilot study, appropriate amendments to the items were made to develop the final draft of the questionnaire.

2.2.3. Phase 3: Assessing known-group validity and reliability

2.2.3.1. Known-group validity assessment. Known-group validity was assessed to determine the significance of the differences between the scores of the groups known to have varying degrees of knowledge about oral anticoagulants (Supplement 1). We involved three different groups of respondents with hypothesized different oral anti-coagulant knowledge levels (i.e., contrasted group approach). The pharmacist group was expected to serve as the positive control while the general public group was expected to serve as the negative control. Consequently, we hypothesized that the mean knowledge score would be highest for the pharmacist group, followed by the patient groups, and then the members of the public group. This approach was also used to develop the original AKT [16].

A target number of 200 samples was recruited for the validation study. To be eligible, the participants had to be aged 18 years or older, understand written Chinese and communicate in Cantonese, and provide informed consent. Stratified sampling was conducted to recruit 50 participants for each of the following four groups.

Group 1 comprised patients who were treated with warfarin and Group 2 comprised patients who were treated with DOACs. Eligible participants for the warfarin and DOAC patient groups were identified from in-house pharmacy dispensing records. They were then randomly selected and approached to participate in this study at the outpatient pharmacy of the QEH. The paper version of the questionnaire was given to the participants after obtaining informed consent, and returned immediately after the questionnaire was completed. The patients completed the questionnaire with minimal guidance from the investigators. The investigators noted down the enquires of patients who had asked for clarifications or had raised questions during the completion of the questionnaires. Patients could return the completed questionnaire as soon as they had completed it, or they were given a maximum of 20 min before the investigators collected the questionnaire from them. This duration (20 min) were chosen assuming that 1 min was taken to answer each question, and that 20 min is a reasonable time frame as this questionnaire is meant to be distributed/completed in a clinical setting. Any incomplete responses were noted by the investigators.

Group 3 comprised registered and practicing pharmacists. Eligible participants for the pharmacist group were recruited using convenience sampling. An email invitation was sent through professional networks and organizations. The paper version of the questionnaire was mailed to the participants, who completed it remotely and returned it to the investigators using a stamped return envelope. The pharmacists were advised to complete the questions independently without referring to any external references.

Group 4 comprised members of the public who were not undergoing treatment with any oral anticoagulants, did not have any close relatives in the same residence taking oral anticoagulants, and were not healthcare providers. Eligible participants in the general public group were randomly recruited using convenience sampling on the streets of five randomly selected major districts in Hong Kong, namely Mong Kok, Fanling, Wong Tai Sin, Causeway Bay, and Kwun Tong. The paper version of the questionnaire was given to the participants and returned immediately after the questionnaire was completed, with minimal guidance. The administration procedures were similar to what was described in the patient group.

An independent-samples Kruskal–Wallis test was used to compare the mean scores of the four participant groups. As previous studies have shown that specialized counselling and individual care from pharmacists can effectively improve patients' knowledge of oral anticoagulants [11,31], we also hypothesized that the mean knowledge score would be higher for patients who attended the PAC than those who received routine care.

2.2.3.2. Reliability assessment. Internal consistency was measured by assessing the intercorrelations of questionnaire items using Cronbach's alpha coefficient [26] (Supplement 1). Cronbach's alpha is one of the most commonly used statistics in research involving test construction and use to the extent that its use in research with multiple-item measurements is considered routine [32]. It is a common practice in medical education research when multiple-item measures of a concept or construct are employed [33]. Cronbach's alpha coefficient values range from 0 to 1, with a value closer to 1 indicating greater consistency. Generally, a value >0.70 reflects adequate internal consistency [33].

3. Results

3.1. Phase 1: Development of the C-OAKT

Nineteen questions were selected from the question bank by the PAC pharmacists. The final questionnaire comprised 14 mandatory questions for all patients and five extended questions for warfarin patients only (Table 2). The computed I-CVIs of all individual items were > 0.80 and the k* values were > 0.79. The overall CVI was 0.95 (Table 2), suggesting that the expert panel perceived all of the items on the questionnaire as valid and relevant.

Table 2
Item and Scale Content Validity Indexes.

Item	General questions	Response options	I-CVI	Modified kappa (k*)[a]
1	What is the name of your anticoagulant medicine?	Multiple choices	1.00	1.00
2	Why did your doctor prescribe this anticoagulant medicine?	Open-ended	1.00	1.00
3	How many times a day do you take this anticoagulant medicine?	Open-ended	0.90	0.90
4	How long (in months) are you required take this anticoagulant medication?	Open-ended	1.00	1.00
5	Is it safe to take Aspirin or NSAIDs while you are taking this anticoagulant medicine?	Yes/no & Open-ended	1.00	1.00
6	Which of the following conditions require you to go to the Accident & Emergency Department immediately?	Multiple choices	1.00	1.00
7	What would you do if you miss a dose of your anticoagulant medicine?	Open-ended	0.90	0.90
8	Is it safe to take vitamin K supplements or foods rich in vitamin K without consulting your doctor?	Yes/no	1.00	1.00
9	What is the most serious side effect of your anticoagulant medicine?	Open-ended	0.90	0.90
10	Will skipping one dose of your anticoagulant medicine worsen your condition?	Yes/no	0.90	0.90
11	Should you stop taking your anticoagulant medicine once you feel better without consulting your doctor?	Yes/no	1.00	1.00
12	Is it necessary to inform a surgeon, dentist or pharmacist that you are taking this anticoagulant medicine before the surgery or procedure?	Yes/no	0.90	0.90
13	What should you do if you accidentally overdose yourself with the anticoagulant medicine?	Open-ended	0.80	0.79
14	What should you do if you are running out of your anticoagulant medicine?	Multiple choices	1.00	1.00
Question specific to patients treated with warfarin				
15	What is your target INR range?	Open-ended	1.00	1.00
16	Are routine INR tests necessary for patients treated on your anticoagulant medicine?	Yes/no	0.80	0.79
17	What may happen if you over-consume dark green vegetables while you are on this anticoagulant medicine?	Multiple choices	1.00	1.00
18	What is one serious consequence that may happen if your INR value is below the target range?	Open-ended	0.90	0.90
19	Which should you do if you have a medication that may interact with warfarin?	Multiple choices	1.00	1.00

I-CVI: Item-Content Validity Index; INR: international normalized ratio; NSAID: non-steroidal anti-inflammatory drugs.

3.2. Phase 2: Pilot study

All 20 participants (response rate: 100%) completed the questionnaire independently with minimal guidance from the investigators. The average time taken to complete the questionnaire was 12.75 min. The mean scores (± standard deviation [SD]) were 91.4 ± 9.56 points, 58.6 ± 24.00 points, and 40.7 ± 12.23 points for the pharmacist group, patient groups, and general public group, respectively.

Amendments were made after receiving feedback from the participants (Supplement 2). First, it was observed that some participants selected more than one option when they were uncertain. Therefore, the instruction "*Please choose only one option for each question*" was added to the questionnaire to improve clarity. Second, an option of "*Not sure*" was added to the questionnaire to prevent participants from making random guesses. Third, some sentence structures were revised to improve their readability (Supplement 2).

The final version of the C-OAKT in Chinese and the corresponding English version are presented in Supplement 3 and 4, respectively.

3.3. Phase 3: Assessing known-group validity and reliability

The demographic characteristics of the 200 participants in the validation study are presented in Table 3.

3.3.1. Known-group validity

The C-OAKT was able to discriminate between pharmacists, patients, and members of the general public. Overall, the mean knowledge score was highest for the pharmacist group (mean ± SD, 90.0 ± 7.11 points), followed by the patient groups (51.55 ± 17.49 points), and the general public group (19.00 ± 15.42 points; $p < 0.001$; Fig. 1A). In addition, the mean knowledge score was significantly higher for patients who attended the PAC (56.80 ± 13.60 points) than those who did not attend the PAC (46.30 ± 19.43 points; $p = 0.004$; Fig. 1B).

The proportion of correct responses for each item, stratified by participant groups, is presented in Table 4. The pharmacist group consistently had >90% of the respondents providing correct responses, while only one third of participants from the general public group provided the correct responses for most questions. In the patient groups, the responses were poorest for questions about the concomitant use of warfarin/DOACs and aspirins and non-steroidal anti-inflammatory drugs (NSAIDs; Question 5) and actions to take when a drug–drug interaction is suspected (Question 9). These two questions belong to the

Table 3
Demographic Characteristics of Respondents.

Characteristics	Members of the public (n = 50)	Warfarin patient (n = 50)	DOAC patient (n = 50)	Pharmacist (n = 50)
Response rate (%)	33.3%	76.9%	83.3%	100%
	n (%)	n (%)	n (%)	n (%)
Gender				
Male	27 (54)	19 (38)	30 (60)	23 (46)
Female	23 (46)	31 (62)	20 (40)	27 (54)
Age, n (%)				
<40 years	21 (42)	1 (2)	0 (0)	48 (96)
40–59 years	13 (26)	8 (16)	7 (14)	2 (4)
60–79 years	14 (28)	40 (80)	31 (62)	0 (0)
≥80 years	2 (4)	1 (2)	12 (24)	0 (0)
Education, n (%)				
Primary school or below	12 (24)	23 (46)	19 (38)	0 (0)
Secondary school	24 (48)	22 (44)	26 (52)	0 (0)
Bachelor degree	14 (28)	4 (8)	3 (6)	18 (36)
Post graduate	0 (0)	1 (2)	2 (4)	32 (64)
Follow up with PAC, n (%)				
PAC	NA	25 (50)	25 (50)	NA
Non-PAC	NA	25 (50)	25 (50)	NA
Time in treatment, n (%)				
<1 year	NA	1 (2)	6 (12)	NA
1–5 years	NA	8 (16)	29 (58)	NA
6–10 years	NA	16 (32)	10 (20)	NA
≥10 years	NA	25 (50)	5 (10)	NA

DOAC: direct-acting oral anticoagulants; NA: Not applicable; these items are not applicable to pharmacists and members of the public; PAC: Pharmacist-led anticoagulation clinic.

category of drug–drug interactions. Between the non-PAC and PAC patients, the largest differences in the proportion of correct responses were observed for questions related to dosing (Question 3; 68% vs. 80%) and identifying symptoms that require immediate medical attention (Question 6; 60% vs. 90%).

3.3.2. *Internal consistency*

The overall Cronbach's alpha value for the 19-item questionnaire was 0.86, and the Cronbach's alpha value for the patient group was 0.77, which indicated that this questionnaire attained good internal consistency.

4. Discussion

This is the first study to evaluate the psychometric properties of a Chinese version of an oral anticoagulation knowledge assessment tool in the Chinese population. Our results revealed that the C-OAKT is valid and reliable, to a great extent, in assessing patients' knowledge of anticoagulants in an ambulatory care setting in Hong Kong.

The content validity was rated highly by the expert panel consisting of specialists in cardiology, internal medicine, and neurology and PAC pharmacists, which indicated that the questions were clinically relevant. The C-OAKT covered all major topics that are essential for patients to know, including questions about indications and instructions regarding the use of DOACs, drug–drug/food interactions, and side effects and their management. This information is important for improving clinical outcomes for patients taking DOACs. A study in Hong Kong revealed that 65% of patients with atrial fibrillation taking warfarin had an INR value that was not within the therapeutic range [34]. Our pilot validation study showed that at baseline, the patients demonstrated a knowledge deficit in drug–drug and drug–food interactions, which can greatly affect the time in the therapeutic range of the INR value. This suboptimal INR control increases the risk of all-cause mortality in patients with atrial fibrillation, making them vulnerable to developing hemorrhagic or ischemic stroke. This tool can potentially be applied in clinical settings to identify knowledge gaps or misconceptions that patients have regarding their oral anticoagulants.

Currently there are some validated tools to evaluate knowledge about anticoagulants. The best-established tool is the OAK developed by Zeolla et al. [14], which was validated in 2006. However, it assesses knowledge of warfarin only. A comparison of the OAK, the AKT [16], and the newly developed C-OAKT is shown in Table 1. The construct validity test did not involve a pharmacist group as an expert group in the evaluation of the OAK. The C-OAKT has an advantage over the OAK, as it involved three different groups. Therefore, the C-OAKT may be more sensitive to multiple levels of anticoagulation knowledge. In addition to multiple-choice questions, the C-OAKT includes open-ended questions, which can precisely test the patients' ability to recall certain factual details regarding their treatment. The number of items in the C-OAKT is smaller than the number of items in the other two tools. Hence, it may be more convenient to use in clinical settings, especially in public hospitals in Hong Kong where the patient load is heavy. To summarize, the C-OAKT is potentially an appropriate screening tool to identify patients who are deficient in their anticoagulant knowledge in Hong Kong.

The C-OAKT demonstrated reasonably good reliability (Cronbach's alpha value = 0.86 for the overall cohort) and the items correlated well with the overall scale. The reliability was slightly lower among the patient group (Cronbach's alpha value = 0.77). This may be because patients scored particularly low marks for some items, including questions about drug interactions with NSAIDs. This pilot validation study did not assess test–retest reliability, as the feasibility of doing so was hindered by the COVID-19 pandemic. It was difficult to contact the patients, as they were reluctant to return to the hospital for follow-up visits. Furthermore, the patients may have tended to determine the correct answer from the Internet or their doctors after the first test; hence, they may have had a better knowledge score in the retest, resulting in low test–retest reliability.

Encouragingly, the C-OAKT was able to differentiate, to a certain extent, the knowledge level of patients who attended the PAC from the knowledge level of those who received routine care. Specifically, the PAC patients had higher scores than the non-PAC patients for questions related to drug–drug/food interactions and side effects. It is reasonable to assume that, as there is more time for pharmacists to explain the drug–drug interactions and side effects in a PAC consultation, the PAC patients had a better understanding of the interactions of oral anticoagulants and how to manage potential adverse reactions. Our validation study also identified certain knowledge gaps among patients. It was observed that the mean knowledge scores obtained for questions about drug–drug interactions and missed dose management were relatively low. Several other studies have reported similar results, with patients' knowledge of drug–drug interactions weaker than their knowledge of other aspects, such as side effects [35-38]. It is worth educating patients about drug–drug interactions, as they may encounter them in daily life. For example, it is common for patients in Hong Kong to purchase over-the-counter cold and flu medications containing NSAIDs, which may increase the risk of bleeding. Through the use of the newly developed C-OAKT, we were able to identify such pertinent knowledge gaps and reinforce education about these aspects. As there is evidence that anticoagulant knowledge is positively correlated with drug adherence [39] and anticoagulant control [11], a larger-scale study is warranted in the future to explore the impact of patient knowledge on downstream clinical outcomes using the C-OAKT as the assessment method.

There are several limitations to consider when interpreting the findings of this study. Although the study site was a major public hospital within the Kowloon region, this was a single-centered study and our results cannot be generalized to other patients who have received oral anticoagulants in Hong Kong. However, all public hospitals in Hong

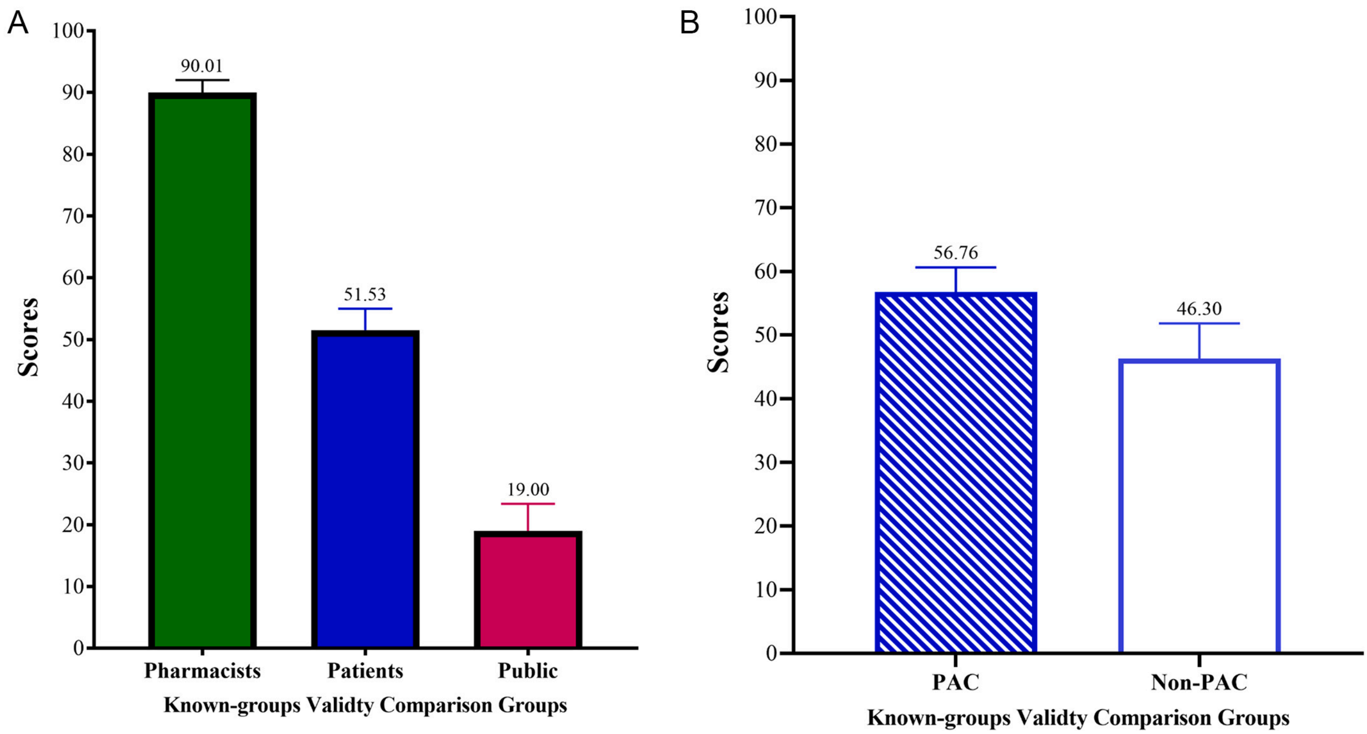

Fig. 1. Comparison of Scores Across Known-Groups Validity Groups. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
1A Comparison of Knowledge Scores Across Pharmacists, Patient on Warfarin/DOAC, and Members of the Public.
Green: Pharmacist group ($n = 50$).
Blue: Patient group ($n = 100$, of whom 50 respondents were on warfarin and 50 were on direct-acting oral anticoagulants).
Red: Members of the public ($n = 50$).
The post-hoc analysis (after Bonferroni correction) showed that the mean knowledge score of the pharmacist group was significantly higher than the patient group ($p = 0.000$) and members of the public ($p = 0.000$). The patient group scored significantly higher than members of the public ($p = 0.000$).
1B Comparison of Knowledge Scores Across PAC and non-PAC Groups.
PAC: Pharmacist-led anticoagulation clinic.
Blue shaded: Patients who attended PAC.
White: Patients who did not attend the PAC (i.e. patients who received routine care).
The patients who attend the pharmacist-led anticoagulation clinic scored significantly higher than the patients who received routine care ($p = 0.004$).

Kong operate under the auspices of the Hospital Authority; hence, the treatment and ambulatory care provided to patients with thromboembolic events are largely similar across all public hospitals in Hong Kong. It is reasonable to assume that the C-OAKT can also be applied to other hospitals or clinics in the city. Second, the C-OAKT is an assessment of the participants' existing knowledge of anticoagulants; however, we were unable to ensure that all the participants completed the questionnaire independently without referring to resources from the internet or consulting other people. This is especially so for the pharmacist group as they completed it remotely without the presence of the investigators (unlike the patient group and members of the general public). Finally, we acknowledge that our validation sample was small. However, there is no absolute rule governing the sample size for validation studies [40]. Previous studies have suggested that 2 to 20 subjects per item, with an absolute minimum of 100 to 250 subjects, is reasonable [41]. Furthermore, a sample of 200 participants for a 20-item questionnaire is within the recommended subject-to-item ratio of 10 to 13.3 [42].

5. Innovation

Patients' knowledge of oral anticoagulants is important, as it may affect their treatment and clinical outcomes. Currently, there is no Chinese anticoagulant knowledge tool that allows healthcare professionals to effectively assess the knowledge of patients taking both warfarin and DOACs. This study successfully developed and validated the C-OAKT for patients treated with warfarin and/or DOACs in Hong Kong. This oral anticoagulant knowledge tool appears to be valid and reliable, and it can be completed by patients on their own without assistance from other healthcare professionals or staff members. In particular, the C-OAKT is relevant to the Chinese population, as it has culturally adapted questions and wording. This tool is applicable to all patients taking anticoagulants who can read Chinese, and healthcare professionals can use this convenient tool to assess patients' knowledge, regardless of the type of oral anticoagulant they are taking.

We acknowledge that, while this study provides preliminary psychometric data to support the distribution of the C-OAKT in clinical settings, a full-scale validation study is required before it can be applied in research studies. Future studies should evaluate the longitudinal validity and responsiveness of the C-OAKT to changes within patients across separate time points after educational interventions. To facilitate the interpretation of the clinical relevance of score changes, identifying the minimum clinically important difference of the C-OAKT will guide its clinical interpretation by providing recognizable end points and thresholds. Finally, validation studies could be performed on different patient populations and demographics, such as exploring correlations between knowledge and educational level, age, race, and time in the therapeutic range, to support the use of the C-OAKT in various clinical and research settings.

6. Conclusions

This oral anticoagulant knowledge tool is the first validated

Table 4
Proportion of Respondents who Provided the Correct Responses.

Item	Proportion of Respondents who Provided a Correct Response for Each Item			
	Members of the public (%)	Non-PAC patients (%)	PAC patients (%)	Pharmacist (%)
Item 1	NA	90	96	NA
Item 2	NA	54	34	NA
Item 3	NA	68	80	NA
Item 4	NA	34	34	NA
Item 5	4	15	37	90
Item 6	2	60	90	100
Item 7	20	12	16	96
Item 8	2	24	46	100
Item 9	12	36	54	100
Item 10	14	12	28	34
Item 11	34	78	92	100
Item 12	68	94	98	100
Item 13	34	14	22	100
Item 14	68	78	90	100
The following questions are for patients on warfarin only.				
Item 15	NA	14	8	NA
Item 16	2	40	50	82
Item 17	2	20	30	96
Item 18	0	18	16	92
Item 19	2	6	22	68

NA = Not applicable; these items are not applicable to pharmacists and members of the public.
PAC: Pharmacist-led anticoagulation clinic.

instrument in Chinese that can be used to assess the anticoagulation knowledge of patients taking warfarin or DOACs. The validation data suggest that it is a valid and reliable tool for assessing various knowledge levels of anticoagulation in Chinese patients. Future research should examine the relationship between patients' knowledge and their anticoagulation control.

Declaration of Competing Interest

All authors do not have any conflict of interest to declare.

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Appendix A. Supplementary data

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