Accuracy of Kampo Diagnostic Support System: Comparison With Certified Physicians of the Japan Society for Oriental Medicine

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Objective: Japanese Traditional (Kampo) Medicine (JTM) relies on traditional diagnostic patterns (*sho*). However, half of Japanese physicians do not consider Kampo patterns when prescribing, increasing the risk of improper use and adverse events. This study evaluated the accuracy and challenges of KAMPO365, a diagnostic support system for JTM, by comparing its outputs with diagnoses and prescriptions by certified physicians of the Japan Society for Oriental Medicine.
Methods: Twenty outpatients at two hospitals participated by inputting clinical data into KAMPO365, which generated Kampo pattern diagnoses and formula recommendations. Specialists, blinded to KAMPO365 outputs, conducted independent diagnoses and prescribed five candidate Kampo formulas.
Results: The results showed a 35% concordance rate between KAMPO365-recommended formulas and specialists' selections, with higher agreement in pharmacological classification (45%). Concordance rates for diagnostic patterns were 55% for deficiency/excess and 65% for cold/heat. For qi, blood, and fluid disturbance patterns, fluid retention had the highest concordance (75%), while qi counter flow and blood deficiency had the lowest (30%).
Conclusion: KAMPO365 demonstrated potential in aiding non-specialists, though improvements in diagnostic algorithms and the coverage of Kampo formulas are needed. Despite its limitations, this study suggests the potential utility of KAMPO365 for diagnosing Kampo patterns and providing precise prescriptions.

Key words: diagnostic support system, integrative medicine, Japanese Traditional (Kampo) Medicine, Kampo formula, Kampo pattern

INTRODUCTION

Japanese Traditional (Kampo) Medicine (JTM) is a traditional form of Japanese medicine. Because 148 ethical Kampo formulas, which are medical Kampo extract formulations, as well as 187 crude drugs are covered by Japanese national health insurance, most Japanese physicians prescribe Kampo formulas in their daily clinical practice [1]. Kampo formula prescriptions are typically based on a traditional diagnostic pattern called *sho* in Japanese [2, 3]. However, a recent survey reported that nearly half of Japanese physicians do not consider Kampo patterns when prescribing Kampo formulas [1]. Inappropriate use of Kampo formulas can increase the risk of adverse events [4, 5]. Furthermore, the number of certified physicians of the Japan Society for Oriental Medicine (JSOM) remains limited, and there are significant challenges in expanding specialized education in this field.

In recent years, medical diagnostic support systems (DSS) have shown potential in enhancing clinical decision-making [6, 7]. Previous studies have reported the efficacy of DSS in improving diagnostic accuracy and medical education [8, 9]. Therefore, DSS may be effective in aiding non-Kampo specialists in prescribing appropriate Kampo formulas. However, few studies have evaluated the effectiveness and challenges of DSS in JTM.

In this study, we evaluated the accuracy and challenges of a Kampo DSS by comparing its diagnostic outputs with those of Kampo specialists.

MATERIALS AND METHODS

Study design

We conducted a prospective exploratory observational study from January 1 to August 31, 2024 (Fig. 1). Participants were new outpatients in the Department of Kampo Medicine at Aizu Medical Center or Tokai University Hospital. After providing documented informed consent, patients accessed KAMPO365, a Kampo DSS, via their smartphones or tablets to input their clinical information and responses to basic questionnaires for Kampo diagnosis. Based on this information, KAMPO365 generated Kampo patterns and recommended Kampo formulas.

After patients completed their inputs, two certified

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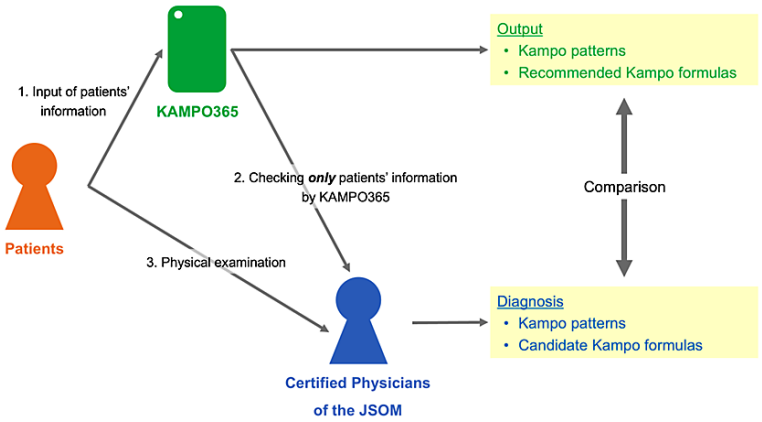

Fig. 1 Study flow chart.
JSOM, Japan Society for Oriental Medicine.

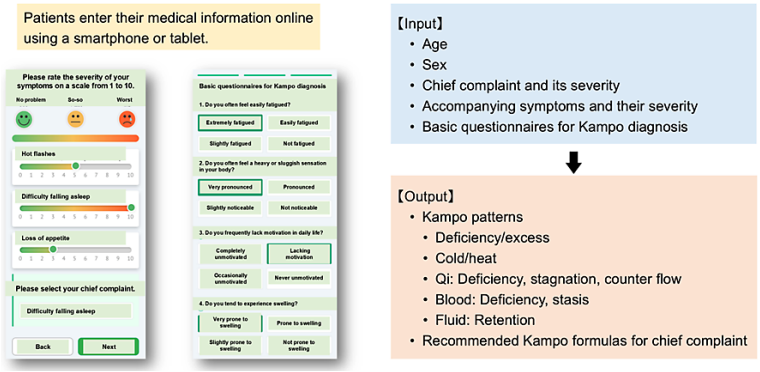

Fig. 2 Conceptual schema of KAMPO365.

physicians of the JSOM accessed the KAMPO365 online platform to review only the patients' information and responses to the basic questionnaires. Notably, the specialists were blinded to KAMPO365's diagnostic outputs and Kampo formula recommendations during the study. The Kampo specialists then conducted Kampo physical examinations. Based on the integrated patient responses and physical examinations, they diagnosed the patients' Kampo patterns and selected five Kampo formula candidates.

Upon completing data collection, we compared the KAMPO365 outputs with the specialists' diagnoses and candidate Kampo prescriptions. This clinical study was approved by the ethical committee at Fukushima Medical University (REC2023-199) and was pre-registered with the University Hospital Medical Information Network (UMIN000054096).

Study population

We set a sample size of 20 patients based on the enrollment period because our study was a pilot trial. We recruited outpatients from the Department of Kampo Medicine at Aizu Medical Center or Tokai University Hospital. The inclusion criteria were as follows: written informed consent to participate in the study, age of ≥ 18 years, and adequate ability to operate smartphones or tablets. Patients currently taking Kampo formulas were excluded from the study.

DSS

We utilized KAMPO365 (VARYTEX Inc., Tokyo, Japan) as the Kampo DSS for this study (Fig. 2). Patients accessed the system online via personal smartphones or tablets and entered their information, including age, sex, chief complaints, accompanying symptoms, and responses to a basic questionnaire composed of approximately 40 items for Kampo diagnosis (Supplementary Tables S1 and S2). Based on this input, KAMPO365 suggested Kampo patterns (*sho*) and recommended Kampo formulas. A list of Kampo formulas covered by KAMPO365 is provided in Supplementary Table S3.

In this study, the Kampo specialists were blinded to the diagnostic outputs from KAMPO365 until the study was completed.

Primary endpoint

The primary endpoint was the concordance rate between the Kampo formulas recommended by KAMPO365 and those selected by certified physicians of the JSOM. Concordance was defined as follows: the Kampo formula recommended by KAMPO365 matched one of the five Kampo formula candidates selected by specialists (one Kampo formula prescribed by specialists and four differential candidates), or the pharmacological classification of the recommended Kampo formula by KAMPO365 matched that of a Kampo formula prescribed by specialists (Supplementary Table S3).

Secondary endpoints

The secondary endpoint was the concordance rate between the Kampo patterns (deficiency/medium/excess, cold/heat, qi deficiency, qi stagnation, qi counter flow, blood deficiency, blood stasis, and fluid retention) generated by KAMPO365 and those diagnosed by specialists.

RESULTS

Patient characteristics

The characteristics of the 20 patients enrolled in this study are shown in Table 1. Eleven patients were from Aizu Medical Center, and nine were from Tokai University Hospital. Their mean age was 47 years, and 90% of the participants were female. Chief complaints included fatigue ($n = 5$), abnormal temperature sensations such as cold intolerance or hot flashes ($n = 4$), gastrointestinal symptoms ($n = 3$), and headache ($n = 3$).

Kampo formula selections between KAMPO365 and specialists

Table 2 compares the Kampo formulas recommended by KAMPO365 with those chosen by Kampo specialists. The concordance rate between the Kampo formulas recommended by KAMPO365 and those selected by certified physicians of the JSOM was 35% (Fig. 3). Additionally, 45% of the Kampo formulas recommended by KAMPO365 matched the pharmacological classification of the formulas prescribed by specialists.

Three of the four cases involving abnormal temperature sensations demonstrated concordance. Among cases with gastrointestinal symptoms, the Kampo formulas recommended by KAMPO365 achieved concordance in two of three patients. However, no concordance was observed among cases of fatigue, which were the most common in our study. Furthermore, certified physicians of the JSOM prescribed Kampo formulas that were not included in the recommendations of KAMPO365 for two patients.

Comparison of Kampo patterns: Deficiency/excess and cold/heat

Table 3 shows all diagnoses for deficiency/excess and cold/heat patterns. The concordance rate for deficiency/excess patterns was 55% (Fig. 4a). Three degrees of deficiency/excess patterns were used in this study. Among the nine mismatch cases, KAMPO365 misjudged only two patients with excess patterns as having deficiency patterns. The remaining seven cases involved discrepancies between medium patterns and either deficiency or excess patterns.

For cold/heat patterns, the concordance rate was 65% (Fig. 4b). KAMPO365 almost correctly identified cases of cold patterns diagnosed by specialists. However, discordances were observed in patients where specialists diagnosed heat patterns and prescribed Kampo formulas such as shigyakusan, kamishoyosan, or nyoshinsan.

Comparison of Kampo patterns: Qi, blood, and fluid disturbance

Table 4 shows diagnoses for qi, blood, and fluid disturbance patterns by KAMPO365 and certified physicians of the JSOM.

For qi disturbance patterns, the concordance rates were 50% for qi deficiency, 60% for qi stagnation, and 30% for qi counter flow (Fig. 5). In 9 of 10 disagreement cases of qi deficiency, KAMPO365 diagnosed a qi deficiency pattern, although the specialists did not. Additionally, KAMPO365 overdiagnosed qi deficiency in two of five cases involving fatigue. In six disagreement cases for qi stagnation, KAMPO365 underestimated the condition. By contrast, KAMPO365 overdiagnosed 13 of 14 mismatch cases involving qi counter flow.

For blood disturbance patterns, the concordance

Table 1 Patients' characteristics

Patients	Age	Gender	Chief Complaint
1	51	Female	Fatigue
2	67	Female	Back pain
3	37	Female	Alternating constipation and diarrhea
4	43	Female	Fatigue
5	64	Female	Cold sensation or hypersensitivity
6	22	Female	Cold sensation or hypersensitivity
7	49	Female	Migraine
8	26	Female	Abdominal pain
9	48	Female	Hot flashes
10	81	Female	Heartburn, acid reflux
11	41	Female	Migraine
12	70	Female	Dizziness
13	63	Male	Fatigue
14	64	Female	Palpitation
15	63	Female	Stiff shoulders
16	19	Female	Depressive feeling
17	57	Female	Tension-type headache
18	34	Female	Fatigue
19	18	Female	Hot flashes
20	30	Male	Fatigue

Table 2 Comparison of Kampo formulas between KAMPO365 and certified physicians of the JSOM

Patients	KAMPO365 output	Certified physicians of the JSOM	
	Recommended Kampo formula	Prescribed Kampo formulas	Candidate Kampo formulas
1 (Groups)	Shokenchuto (Warming and tonifying formula (without processed Aconite Root))	Nyoshinsan (Qi-regulating formula)	Saikokaryukotsuboreito, keishibukuryogan, kamishoyosan, and saikokeishikankyoto
2 (Groups)	Goshakusan (Dual-interior and exterior-releasing formula)	Makyoyokukanto (Not applicable for KAMPO365 output)	Tsudosan, yokuininto, eppikajutsuto, and hachimijiogan
3 (Groups)	Daikenchuto (Warming and tonifying formula (without processed Aconite Root))	Keishikashakuyakuto (Warming and tonifying formula (without processed Aconite Root))	Keishikashakuyakudaioto, shokenchuto, tokikenchuto, and tokishakuyakusan
4 (Groups)	Kamikihito (Qi and blood-tonifying formula)	Hochuekkito (Qi-tonifying formula)	Yokukansan, yokukansankachimpihange, kamishoyosan, and hangekobokuto
5 (Groups)	Hachimijiogan (Warming and tonifying formula (with processed Aconite Root))	Hachimijiogan (Warming and tonifying formula (with processed Aconite Root))	Goshajinkigan, ryokyojutsukanto, shimbuto, and tokishakuyakusan
6 (Groups)	Ninjin'yoeito (Qi and blood-tonifying formula)	Shigyakusan (Harmonizing formula)	Saikokeishikankyoto, kamishoyosan, tokishakuyakusan, and tokikenchuto
7 (Groups)	Goshuyuto (Warming and tonifying formula (without processed Aconite Root))	Shigyakusan (Harmonizing formula)	Saikokeishito, goreisan, kakkonto, and tokishakuyakusan
8 (Groups)	Tokishigyakukagoshuyushokyoto (Warming and tonifying formula (without processed Aconite Root))	Ninjinto (Warming and tonifying formula (without processed Aconite Root))	Keishininjinto, bushirichuto, daikenchuto, and tokishigyakukagoshuyushokyoto
9 (Groups)	Byakkokaninjinto (Heat-clearing formula)	Nyoshinsan (Qi-regulating formula)	Kamishoyosan, orengedokuto, keishibukuryogan, and byakkokaninjinto
10 (Groups)	Hangeshashinto (Harmonizing formula)	Bukuryoin (Fluid-regulating formula)	Bukuryoingohangekobokuto, hangekobokuto, heiisan, and rikkunshito
11 (Groups)	Goshuyuto (Warming and tonifying formula (without processed Aconite Root))	Kamishoyosan (Harmonizing formula)	Saikokaryukotsuboreito, tokakujokito, keishibukuryogan, and tokishakuyakusan
12 (Groups)	Goreisan (Fluid-regulating formula)	Nyoshinsan (Qi-regulating formula)	Hangekobokuto, goreisan, kamishoyosan, and ryokeijutsukanto
13 (Groups)	Kihito (Qi and blood-tonifying formula)	Hangekobokuto (Qi-regulating formula)	Hangebyakujutsutemmato, hachimijiogan, ninjin'yoeito, and juzentaihoto
14 (Groups)	Kamishoyosan (Harmonizing formula)	Bukuryoingohangekobokuto (Fluid-regulating formula)	Bukuryoin, hangekobokuto, hochuekkito, and kihito
15 (Groups)	Tokishakuyakusan (Fluid-regulating formula)	Tokishakuyakusan (Fluid-regulating formula)	Senkyuchachosan, boiogito, hangebyakujutsutemmato, and kihito
16 (Groups)	Kamikihito (Qi and blood-tonifying formula)	Kamikihito (Qi and blood-tonifying formula)	Tokishakuyakusan, hangekobokuto, kihito, and keishikaryukotsuboreito
17 (Groups)	Goreisan (Fluid-regulating formula)	Boiogito (Fluid-regulating formula)	Goreisan, saikokeishikankyoto, kamishoyosan, and hochuekkito
18 (Groups)	Kamikihito (Qi and blood-tonifying formula)	Tokishakuyakusan (Fluid-regulating formula)	Hangebyakujutsutemmato, hochuekkito, bukuryoin, bukuryoingohangekobokuto
19 (Groups)	Kamishoyosan (Harmonizing formula)	Shigyakusan (Harmonizing formula)	Keishibukuryogankayokuinin, saikoseikanto, seijobofuto, and jumihaidokuto
20 (Groups)	Juzentaihoto (Qi and blood-tonifying formula)	Keishimaokakuhanto (Not applicable for KAMPO365 output)	Keishito, keishinieppiitto, saikokeishito, and keishikabushito

JSOM, Japan Society for Oriental Medicine.

rates were 30% for blood deficiency and 45% for blood stasis. In 13 of 14 disagreement cases for blood deficiency, KAMPO365 diagnosed a blood deficiency pattern, although the specialists did not evaluate one. Conversely, KAMPO365 underestimated eight cases diagnosed as blood stasis patterns by specialists.

Among qi, blood, and fluid disturbance patterns, the concordance rate for the fluid retention pattern was the highest (75%). KAMPO365 overdiagnosed fluid retention in all inconsistent cases.

DISCUSSION

This is the first study to evaluate the diagnostic accuracy of a DSS in JTM by directly comparing it with certified physicians of the JSOM. The three key findings are as follows. First, the concordance between KAMPO365-recommended Kampo formulas and specialists' decisions was approximately 40%. Second,

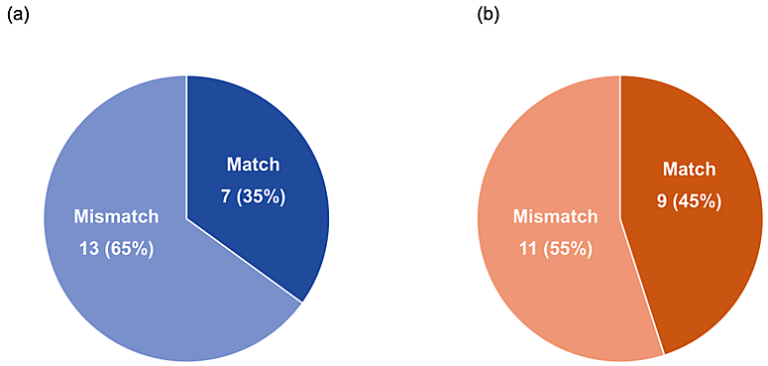

Fig. 3 The concordance ratio of Kampo formulas between KAMPO365 and Kampo specialists.
(a) Concordance between the Kampo formulas recommended by KAMPO365 and those selected by specialists. (b) Concordance of the pharmacological classification of Kampo formulas recommended by KAMPO365 and those chosen by specialists.

Table 3 Comparison of deficiency/excess and cold/heat patterns between KAMPO365 and certified physicians of the JSOM

Patients	Deficiency/excess		Cold/heat	
	KAMPO365	Physicians	KAMPO365	Physicians
1	Deficiency	Excess	Heat	Heat
2	Medium	Excess	Heat	Heat
3	Medium	Medium	Cold	Cold
4	Deficiency	Deficiency	Cold	Heat
5	Medium	Deficiency	Cold	Cold
6	Deficiency	Medium	Cold	Heat
7	Medium	Medium	Cold	Heat
8	Deficiency	Deficiency	Cold	Cold
9	Medium	Medium	Heat	Heat
10	Excess	Medium	Heat	Heat
11	Deficiency	Medium	Cold	Heat
12	Medium	Medium	Cold	Heat
13	Medium	Deficiency	Cold	Cold
14	Deficiency	Deficiency	Cold	Cold
15	Deficiency	Deficiency	Cold	Cold
16	Deficiency	Deficiency	Heat	Cold
17	Medium	Medium	Heat	Cold
18	Deficiency	Deficiency	Cold	Cold
19	Deficiency	Excess	Heat	Heat
20	Medium	Excess	Heat	Heat

JSOM, Japan Society for Oriental Medicine.

KAMPO365 achieved a concordance rate of > 50% in deficiency/excess and cold/heat patterns compared with specialists. Third, among qi, blood, and fluid disturbance patterns, qi counter flow and blood deficiency showed the lowest concordance rates, while the fluid retention pattern exhibited the highest.

Few randomized controlled trials have examined the direct relationship between Kampo pattern-based diagnosis and the safety of Kampo formulas. However, several clinical studies have assessed the efficacy and safety of Kampo formulas using sho-based stratified designs. For example, one study reported that Orengedokuto, an excess-pattern formula, was associated with an increased incidence of adverse events in deficiency-pattern patients [4]. In contrast, another clinical trial limited to excess-pattern patients demonstrated the efficacy and safety of Orengedokuto [5]. These results indirectly support the clinical advantage of Kampo pattern-based pattern differentiation.

A recent online survey revealed that Japanese physicians are concerned that Kampo formula prescriptions without pattern-based consideration may fail to achieve satisfactory therapeutic outcomes [1]. Despite limitations in diagnostic support capability, KAMPO365 can provide assisted diagnostic outputs for physicians who do not routinely consider Kampo patterns. In our study, KAMPO365 showed less than half the accuracy of Kampo formula selections compared with specialists. The clinical decision-making for Kampo formula prescriptions depends on the diagnosis of Kampo

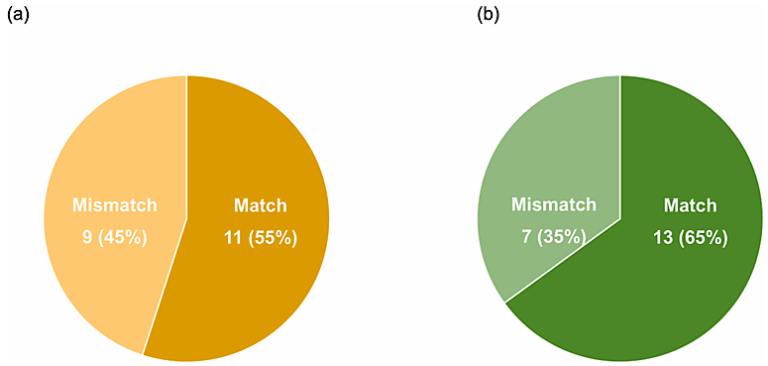

Fig. 4 The concordance ratio of deficiency/excess patterns and cold/heat patterns between KAMPO365 and Kampo specialists. (a) Deficiency/excess patterns. (b) Cold/heat patterns.

Table 4 Comparison of qi, blood, and fluid disturbance patterns between KAMPO365 and certified physicians of the JSOM

Patients	Qi deficiency		Qi stagnation		Qi counter flow		Blood deficiency		Blood stasis		Fluid retention	
	KAMPO365	Physicians	KAMPO365	Physicians	KAMPO365	Physicians	KAMPO365	Physicians	KAMPO365	Physicians	KAMPO365	Physicians
1	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
2	Yes	No	No	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes
3	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	No
4	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes
5	Yes	Yes	No	No	No	No	No	Yes	No	No	Yes	Yes
6	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes
7	No	No	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes
8	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
9	Yes	No	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes
10	No	No	No	Yes	No	Yes	No	No	Yes	No	Yes	Yes
11	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No
12	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No
13	Yes	Yes	No	Yes	Yes	No	Yes	No	No	No	No	No
14	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No
15	Yes	No	Yes	No	Yes	No	Yes	Yes	No	No	Yes	Yes
16	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
17	Yes	Yes	Yes	No	No	No	Yes	No	No	Yes	Yes	Yes
18	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes
19	Yes	No	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	No
20	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	No

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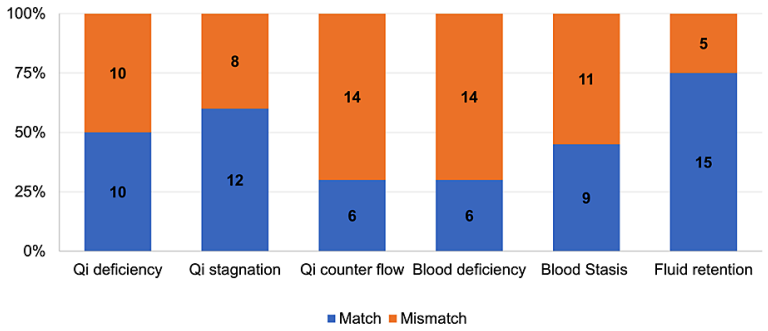

Fig. 5 The concordance ratio of qi, blood, and fluid disturbance patterns between KAMPO365 and Kampo specialists.

patterns, particularly deficiency/excess and cold/heat patterns [3, 10, 11]. Therefore, KAMPO365's diagnostic accuracy for Kampo patterns must be improved to better guide Kampo prescriptions. Additionally, specialists prescribed Kampo formulas that were not covered by KAMPO365 in two cases. Future improvements should aim to expand the types of Kampo formulas recommended by KAMPO365 to include all formulas covered by the Japanese health insurance system.

Among the inconsistent cases regarding deficiency/excess patterns, only two patients (10%) with an excess pattern were misdiagnosed as having a deficiency pattern by KAMPO365, which increases the clinical risk of adverse events from Kampo formulas. One study showed that approximately 40% of new outpatients at JTM departments were coded as having a medium pattern [10]. Therefore, the diagnostic accuracy for medium patterns is critical for the clinical use of KAMPO365. Additionally, in the most common case of fatigue in this study, the Kampo formulas recommended by KAMPO365 and those selected by specialists did not match. Fatigue is one of the most typical symptoms for which Kampo formulas are prescribed [1]. In addition, it has been reported that Kampo medical diagnoses for fatigue may involve not only deficiency patterns but also excess patterns [12, 13]. For fatigue, the most common complaint in our study, KAMPO365 recommendations showed no concordance with specialist prescriptions. Improving the accuracy of KAMPO365 in diagnosing deficiency, medium, and excess patterns is essential for providing adequate Kampo treatment for patients with fatigue.

Cold/heat pattern diagnoses exhibited higher concordance compared to deficiency/excess patterns. However, discrepancies were observed in cases where Kampo specialists prescribed Kampo formulas for patients with heat patterns and obvious localized cold sensations, such as pathophysiological conditions targeted by shigyakusan [14]. Because KAMPO365 generates Kampo medical diagnoses based on subjective interview information entered by patients, it is possible that patients were unable to accurately report their localized abnormal temperature sensations or hypersensitivities. Additionally, specialists may supplement this information through physical examinations in JTM, enabling more accurate diagnoses and prescriptions. It has been suggested that KAMPO365 should incorporate measures, such as thermography, to improve its diagnostic accuracy for cold and chill in patients experiencing localized abnormal temperature sensations or hypersensitivities [15].

In clinical situations, Kampo abdominal examination is one of the most meaningful skills for precise diagnosis [13, 16–18]. Our results indicated that KAMPO365 tended to underestimate qi stagnation and blood stasis patterns while overestimating qi counter flow and blood deficiency patterns. These disturbances were possibly related to typical abdominal signs, such as "fullness and discomfort in the chest and hypochondrium" for qi stagnation pattern, "para-umbilical tenderness and resistance" for blood stasis pattern, "epigastric aortic pulsation" for qi counter flow pattern, and "dry skin" for blood deficiency pattern [16]. Educational training models of typical Kampo abdominal signs are already available [18], and simulators are useful for medical education [19, 20]. Therefore, even when non-Kampo specialists utilize KAMPO365, it may be possible to improve diagnostic accuracy by combining it with information from Kampo abdominal examinations.

Our study has several limitations. First, it was not designed as a parallel trial. Second, our study was a pilot trial and only a few patients were recruited. Therefore, the unbalanced male-to-female ratio may have affected the accuracy of concordance between specialists and KAMPO365. Third, we were unable to evaluate all chief complaints supported by KAMPO365. Fourth, the inter-rater reliability (IRR) of JTM diagnoses, even between Kampo specialists, is challenged by ununified diagnostic approaches [21, 22]. However, a recent report indicated that the diagnostic modularization approach determined by deficiency/excess, cold/heat, and qi, blood, and fluid patterns improved the IRR in Kampo pattern diagnoses [22]. Therefore, KAMPO365 potentially enhances the IRR and promotes accurate Kampo formula prescriptions by physicians regardless of their expertise in JTM. Further clinical data accumulation is warranted to improve the diagnostic quality of KAMPO365.

In conclusion, this study demonstrates the potential utility of KAMPO365, a DSS in JTM, while highlighting areas for improvement to enhance its clinical applicability.

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AUTHORS' CONTRIBUTIONS

KU, TY, HI, SI, and TN designed the study. KU drafted the manuscript. KU and TN conducted the clinical study to obtain the data. KU performed the analyses. TY, HI, SI, and TN critically reviewed and revised the manuscript. TN supervised the entire study. All authors read and approved the final version of the manuscript.

DATA AVAILABILITY

All data are included in this article. For further inquiries, please contact the corresponding author.

CONFLICT OF INTEREST

KU received research grant support from TSUMURA & CO. and SEIRIN. TY was employed at Keio University for collaborative research with TSUMURA & CO. TN received lecture fees from TSUMURA & CO. and Kracie, Ltd. The authors declare that this research was conducted without any commercial or financial relationships that could be construed as potential conflicts of interest.

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Supplementary Table S1 Chief complaints and accompanying symptoms covered by KAMPO365

General Physical Symptoms	Hot flashes Warm sensation or hypersensitivity Cold sensation or hypersensitivity Simultaneous occurrence of cold and warm sensations Excessive sweating Swelling Vertigo and dizziness Palpitation Tendency to gain weight Shoulder stiffness Fatigue or lethargy Lower back pain
Headaches	Migraine Tension-type headache
Mental Symptoms	Depressed mood Irritability Anxiety
Sleep Disorders	Difficulty falling asleep Frequent awakenings during the night Early morning awakening with inability to return to sleep
Gastrointestinal Symptoms	Abdominal pain (including bloating) Diarrhea Constipation Alternating diarrhea and constipation Loss of appetite Indigestion (dyspepsia) Stomach pain Heartburn, acid reflux Gastritis
Gynecological Symptoms	Menstrual pain (dysmenorrhea) Premenstrual syndrome (PMS) Irregular menstruation

Supplementary Table S2 KAMPO365 basic questionnaire for Kampo diagnosis

Questions	Choices
1. Do you often feel easily fatigued?	Extremely fatigued Easily fatigued Slightly fatigued Not fatigued
2. Do you often feel a heavy or sluggish sensation in your body?	Very pronounced Pronounced Slightly noticeable Not noticeable
3. Do you frequently lack motivation in daily life?	Completely unmotivated Lacking motivation Occasionally unmotivated Never unmotivated
4. Do you tend to experience swelling?	Very prone to swelling Prone to swelling Slightly prone to swelling Not prone to swelling
5. Do you experience motion sickness?	Very frequently Frequently Occasionally Never
6. Do you experience dryness of the skin?	Very prone to dryness Prone to dryness Slightly prone to dryness Not prone to dryness
7. Are your nails brittle or prone to breakage?	Very prone to breaking Prone to breaking Occasionally break Never break

8. Have you noticed increased hair loss compared to before?	Significant hair loss Noticeable hair loss Slightly noticeable hair loss No noticeable hair loss
9. Do you tend to have lingering scars or bruises?	Very prone to lingering marks Prone to lingering marks Rarely noticeable Not noticeable
10. Do you frequently experience forgetfulness?	Very frequent Frequent Rare Not frequent
11. Do you often feel abdominal bloating or discomfort?	Very often Often Occasionally Never
12. Are you prone to constipation?	Yes No
13. Have you ever experienced hemorrhoids (including ongoing treatment)?	Frequently Occasionally Never
14. Have you noticed a decrease in your ability to concentrate?	Very pronounced Noticeable Slightly noticeable Not noticeable
15. Do you often feel down or experience depressive moods?	Very frequently Frequently Occasionally Never
16. Are you easily startled by minor things?	Very easily startled Easily startled Rarely startled Not startled
17. Do you often feel a strong sense of anxiety?	Very strong Strong Slightly noticeable Not noticeable
18. Do you often feel impatient or irritable?	Very often Often Occasionally Never
19. Do you tend to feel sleepy after meals?	Very frequently Frequently Occasionally Never
20. Do you find it difficult to wake up and feel sluggish in the morning?	Very applicable Applicable Slightly applicable Not applicable
21. Are you prone to feeling sleepy during the day?	Very prone Prone Occasionally Not prone
22. Please select the option that best describes your appetite:	Excessive appetite Normal appetite Loss of appetite
23. Do you often feel thirsty?	Very frequently Frequently Normal thirst level Not thirsty
24. Please select the option that best describes your experience with belching:	Excessive Frequent None

25. Do you sweat easily?	Very easily Easily Normal Not easily
26. Do you especially sweat on your hands or feet?	Yes No
27. Do you experience night sweats?	Very frequently Frequently Occasionally Never
28. Is your urine darker in color?	Dark Normal Light (transparent)
29. Please select the option that best applies to your temperature preference:	Sensitive to heat Sensitive to cold
30. Do you crave cold drinks or food even in winter?	Yes No
31. Do you crave warm drinks or food even in summer?	Yes No
32. Do you often feel cold?	Very frequently Frequently Occasionally Never
33. Please indicate the area(s) where you feel cold:	Entire body Lower body Hands and feet (extremities) Abdomen
34. Do you experience both cold sensations and hot flashes?	Clearly noticeable Occasionally noticeable Not noticeable
35. Do you feel a heavy sensation in your head?	Very pronounced Pronounced Slightly noticeable Not noticeable
36. Do you feel a sensation of something stuck or discomfort in your throat?	Very pronounced Pronounced Slightly noticeable Not noticeable
37. Do you experience dizziness or lightheadedness?	Very frequently Frequently Occasionally Never
38. Are dark circles under your eyes noticeable?	Very noticeable Noticeable Occasionally noticeable Not noticeable
39. Have you entered menopause?	Yes Approaching menopause No
40. Do blood clots often appear in your menstrual blood?	Very frequent Frequent Occasionally Never
41. Do you have excessive vaginal discharge?	Very frequent Frequent Normal or infrequent

Supplementary Table S3 Groups of Kampo formula candidates recommended by KAMPO365

Groups	Names of Kampo formulas																		
Qi-tonifying formula	Shikunshito	Hochuekkito	Rikkunshito	Keihito															
Blood-tonifying formula	Shimotsuto	Kyukichokeisuin	Shichimotsukokato	Kyukichokeisuin															
Qi and blood-tonifying formula	Juzentaihoto	Ninjinyoeito	Kihito	Kamikihito															
Yin-nourishing formula	Rokumigan	Shakuyakuzoto	Seishoekkito																
Warming and tonifying formula (without processed Aconite Root)	Ninjinto	Keishinin jinto	Anchusan	Tokito		Daikenchuto	Keishikashakuyakuto		Tokishigyakukagoshuyushokyoto	Tokikenchuto		Ogikenchuto	Goshuyuto		Unkeito	Shokenchuto			
Warming and tonifying formula (with processed Aconite Root)	Shinbuto	Hachimijiogan	Goshajinkigan	Bushiirichuto															
Spirit-calming formula	Kanbakutaisoto	Sansoninto	Saikokaryukotsuboreito	Keishikaryukotsuboreito															
Qi-regulating formula	Hangekobokuto	Kososan	Nyoshinsan	Nichiito		Ireito	Yokukansankachimpihange		Yokukansan		Chotosan	Heisan							
Blood stasis-resolving formula	Keishibukuryogan	Tokakujokito	Daiobotampito	Tsudosan		Choyoto	Keishibukuryogankayokuninin												
Fluid-regulating formula	Goreisan	Ryokeijutsukanto	Boiogito	Tokishakuyakusankabushi	Mokuboito	Shohangekabukuryoto			Bukuryoinghangekobokuto		Tokishakuyakusan	Ryokyojutsukanto	Keishikajutsubuto	Nijutsuto	Daibofito				
Exterior-releasing formula	Kakkonto	Keishikakkonto	Senkyuchachosan	Keishikangito												Sokeikakkesuto	Kumibimoto	Bukuryoin	Hangebyakujutsumato
Purgative formula	Daiokanzoto	Daipikito	Choijokito	Keishikashakuyakudaioto	Mashininigan	Junchoto													
Heat-clearing formula	Orengedokuto	Sanoshashinto	Ryutanshakanto	Byakkokaninjinto	Unseiin	Choreito			Sanmotsuregouto		Seishinrenshiin	Inchingoreisan	Otsujito						
Harmonizing formula	Chikujointanto	Saikokeishito	Daisaikokyodaio	Saikokeishikankyoto	Saibokito	Saireito			Shakuyakukanzoto		Shigyakusan	Kamishoyosan	Hangeshashinto	Oren to					
Dual-interior and exterior-releasing formula	Daisaikoto	Bofutsushosan	Goshakusan																