

Short Communication

Comparison of the formulas from the current form of
traditional Japanese pediatrics and those described in
Yoyokasoku (In-house Methods of Pediatrics): A
representative pediatric classic

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Running title: Formulas from Yoyokasoku

ABSTRACT

Aim: There may exist a gap between the current form of traditional Japanese Kampo pediatrics and Kampo pediatrics in the nineteenth century. This study aimed to elucidate changes in clinical practice by comparing the formulas used then and now.

Methods: All formulas described in Yoyokasoku (In-house Methods of Pediatrics [IMP], a Kampo classic published in 1885) and formulas used in a contemporary pediatric Kampo guideline were extracted. Then, a database with annotations to formulas was compiled.

Results: In all, 387 formulas (274 excluding duplications) and 10 methods of moxibustion/surgical treatments were extracted from IMP. The total number of classical formulas described was 72. The proportion of classical formulas was significantly different among disease clusters ($P < 0.0001$). Overall, the contemporary Kampo guideline used classical formulas in any type of disease, and the proportion of this usage was significantly higher than that in IMP (59% vs. 19%, $P < 0.0001$). IMP described 95 Japanese original formulas (25%) including 45 in-house formulas. However, none of them have been implemented in the contemporary guideline.

Conclusion: Current Kampo pediatrics may have developed less under the influence of a pediatric classic in the nineteenth century; however, a thorough investigation of

pediatric books is needed to understand the history of Kampo pediatrics.

KEY WORDS: history of medicine, Japanese Kampo medicine, medical classics, pediatrics, Toshu Murase, Yoyokasoku (in-house methods of pediatrics)

INTRODUCTION

Traditional Chinese medicine (TCM) has a thousand-year history of pediatrics, which has remained an independent specialty to date [1]. At the beginning of traditional Japanese Kampo medicine (JKM) which originated from TCM, the oldest existing Japanese medical classic, *Ishinpo* (Yasuyori Tanba, 984 CE) included a chapter on pediatrics (volume 25) which described pediatric internal and surgical treatments, citing imported Chinese medical textbooks [2]. After the establishment of *Kareishoniho* (Method for Longevity of Children, 1566 CE) written by an internist, Manase Dosan, many books on pediatrics were published in Japan, and pediatrics became independent from internal medicine [3], although Japanese pediatricians seemed to accept adult patients [4]. At the beginning of the Meiji Era, traditional JKM was excluded from orthodox medicine and was integrated into the Western medical system. In 1895, a proposed amendment to the Medical Practitioners' Act was rejected in the Imperial Diet; thereafter, all doctors needed to study Western medicine to become newly licensed [5]. JKM was almost abandoned

and was practiced by few at this time, until recent days when JKM accumulated much clinical and scientific evidence, becoming a required subject included in the Model Core Curriculum for Medical Education (2001 CE) [6].

As JKM revived, pediatric Kampo became popular, using traditional examinations such as abdominal examination, and JKM pattern identification such as qi, blood and fluid pattern, six-meridian pattern, and visceral pattern [7]. Simultaneously, pediatricians evaluated pathogenesis using blood tests and image studies [8, 9]. Based on traditional practice and newly established evidence from randomized controlled trials, most pediatricians prescribe pharmaceutical-grade JKM extract formulas to children [9]. However, more than half of 148 pharmaceutical-grade extracts currently covered by Japan's National Health Insurance (JNHI) are derived from *Shanghanlun* and *Jingui Yaolue* which rarely describe pediatric diseases [10, 11].

Yoyokasoku (In-house Methods of Pediatrics [IMP]) was written by Toshu Murase (1830-1885 CE), who was the physician to the feudal lord in the Owari Clan (now, Nagoya) [12, 13]. He was a well-known and talented Kampo pediatrician to the level that he was appointed by the Meiji Emperor to become a court physician to see his princes and princesses [14]. IMP was published in 1885 and no other textbooks are known to be published between 1885 and 1895 when JKM was abandoned. Thus, IMP seems to

be a representative pediatric Kampo classic which should include many traditional formulas for many disease types.

A gap may exist between the current form of pediatric Kampo and traditional Japanese pediatrics before the nineteenth century, considering the duration from abandonment to revival of JKM is almost a century. However, the formulas described in IMP have not been well studied. Therefore, this study aimed to extract all formulas from IMP and to elucidate the clinical practice of traditional Japanese pediatrics described in IMP. By comparing the formulas from IMP to the formulas frequently used in contemporary pediatric Kampo, we studied whether IMP was influential in establishing the current form of traditional Japanese Kampo pediatrics.

METHODS

Extraction of formulas from the textbooks

Digitized books available to the public from the National Diet Library Digital Collections were used to analyze formulas from IMP [12]. IMP consisted of five volumes in three books the titles of which together formed the verse, ‘Sometimes again reading my books’, from ‘Reading the Book of Hills and Seas’ by Tao Yuanming. The pages of Book 1, which includes the two volumes ‘Sometimes’ and ‘Again’ (DOI: 10.11501/835495),

Book 2, including the two volumes ‘Reading’ and ‘My’ (DOI: 10.11501/835496) and Book 3, including only the one volume of ‘Books’ (DOI: 10.11501/835497), were retrieved. All the formulas described in the Methods sections were extracted and a database was compiled. Surgical treatments and moxibustion were excluded from the analysis. As a control, all 516 formulas were extracted from ‘Shoni Kampo Chiryō no Tebiki’ (Manual of Pediatric Kampo Treatment [MPKT]), an official guideline published by the Japan Pediatric Oriental Medicine Society [7]. The list of the 148 Kampo extract formulas approved by the JNHI was also constructed and annotated.

Defining the origin of the formulas

Regarding IMP, some formulas have a marginal annotation to describe the origin of the formulas; however, some of these were obviously misunderstood by the author, so the origins of formulas were redefined by analyzing the component crude drugs written next to the name of the formulas. Regarding formulas extracted from MPKT and the 148 JNHI-approved formulas, the origin of the formulas was defined using ref [15].

‘Classical formula’ was defined as a formulation recorded in Zhang Zhongjing's works, namely *Shanghanlun* and *Jingui Yaolue*. ‘Modern formula’ was defined as a formula developed after Zhang Zhongjing's works. The formulas developed in Japan and the original combinations of two or more existing extracts were classified as ‘Japanese

originals (honcho keiken ho)'.

Statistical analysis

Statistical analyses were performed using Fisher's exact test for categorical variables. A probability (*P*) value <0.05 was considered to indicate statistical significance. All statistical analyses were conducted using JMP Pro 15.1.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Summary of formulas described in IMP

A total of 387 formulas were described in IMP (Fig. 1; Table S1). The same formulas were described to treat different diseases; thus, there were 274 different formulas excluding duplications. Ten methods of moxibustion and surgical treatments were also described and these were excluded from the further analyses. These are discussed in detail elsewhere [16]. The number of formulas was approximately in proportion to the number of pages from the chapters: in Book 3 the chapter for variola, measles, and chickenpox included 114 formulas (29%); Book 1, chapters for infection and miscellaneous diseases included 108 (28%); in Book 2, the chapters for neurodevelopmental diseases included 78 (20%); also in Book 2, the chapter for neonate and infants included 51 (13%); and in Book 1, the chapter for a local epidemic fulminant enterocolitis called *hayate* included

36 (9%), respectively.

Figure 2a shows the classification of the formulas used according to each disease cluster. The number of classical formulas was 72 (19%) including duplications. The proportion of use of classical formulas was different among disease clusters; the chapter for *hayate* used up to 58% classical formulas, whereas the chapter for neurodevelopmental diseases only used 4%. This difference in the proportion of using classical formulas among disease clusters was significant ($P < 0.0001$).

Comparison of the formulas' usage between IMP and MPKT

Figure 2b shows the classification of the formulas used according to each disease cluster in the contemporary pediatric Kampo described in MPKT. Overall, MPKT used classical formulas in every disease type and this usage was significantly higher than that in IMP (59% vs. 19%, $P < 0.0001$, Tables S1 and S2). The classification of formulas seemed similar between the MPKT and JNHI-approved Kampo formulas, although there was a statistical difference ($P = 0.0385$, Fig. 3). IMP included various traditional disease names that cannot be readily interpreted by contemporary concepts of disease. However, disease entities such as constipation and abdominal pain, enuresis, common cold, and asthma were common between IMP and MPKT. The formulas for these were compared (Table S3) with four common formulas found for constipation and abdominal pain (33% of

formulas from IMP and 21% of formulas from MPKT), none found for enuresis, eight found for common cold (30% for IMP and 27% for MPKT), and four found for asthma (22% for IMP and 20% for MPKT). All of these common formulas were derived from Shanghanlun and Jingui Yaolue except for rikkunshito for abdominal pain and gokoto and hochuekkito for asthma.

Japanese originals in IMP and MPKT

IMP described 95 Japanese original formulas (25%) including 45 in-house formulas from the Murase family with detailed descriptions (Table S1). This proportion of using Japanese originals was significantly higher than that in the MPKT, which described 84 (16%) Japanese originals ($P = 0.0024$, Table S2). Notably, none of the Japanese originals and in-house formulas in IMP were implemented in the MPKT.

DISCUSSION

This report is the first to fully analyze formulas from IMP. The author of IMP, Toshu Murase, also published a textbook on prescription, 'Hoi Zokucho' (Kampo Formulation Sequel) in 1889 [13]. This book described formulas for treating many internal diseases, suggesting that Murase was also a talented physician for adult patients. This is in line with the historical practice among Japanese pediatricians who saw adult patients as well

as children. Domei Yakazu, a physician who laid the foundation for the revival of the JKM in the twentieth century, attached importance to the formulas described in the Kampo Formulation Sequel. He also focused on IMP, saying, ‘IMP describes many Japanese original methods which may compensate common prescriptions in TCM pediatrics. IMP is the book of a great master pediatrician, describing decoctions as well as moxibustion, which also includes in-house methods of the Murase family who practiced pediatrics for three generations’ [13]. More than half of the formulas, including in-house formulas, provided detailed explanations of their components (215 of 387 formulas). Most of those without descriptions were derived from well-known medical classics such as Shanghanlun, Hejijufang, and Wanbinghuichun (Table S1). Thus, formulas from IMP are reproducible at present although their clinical effects should be evaluated.

From a viewpoint of pediatrics, common diseases then and now are quite different. In the nineteenth century, variola was still a common disease in Japan [17] and its treatment was emphasized as well as many other life-threatening infectious diseases which Western medicine could not properly treat [18]. In the modern age, however, most infections are treated by modern Western medicine, and the JKM pediatrics are often utilized in functional diseases, psychological problems, and mental problems seen in

adolescence, focusing on total care [7]. Another important difference is the disease clusters that utilize classical formulas. In IMP, infectious diseases and gastrointestinal disease including *hayate*, a fulminant form of infectious enterocolitis, were commonly treated with classical formulas. This is acceptable because Shanghanlun was originally developed for acute phases of infections [10]. Conversely, the MPKT frequently used classical formulas in any disease type. This trend may be influenced by the modern general JKM, the method of which may be reflected in the adoption of JNHI-approved formulas. Surprisingly, Murase's in-house formulas and his application of Japanese originals to pediatrics were not at all described in the MPKT. Together, these suggest that there is a gap between traditional Japanese pediatrics of the nineteenth century and contemporary pediatric Kampo.

Due to the limited number of books analyzed, this study may reflect only a part of pediatric Kampo and its changes. Additionally, the frequency of usage of formulas described in the medical books does not necessarily correlate with that of prescription in the real world. Thus, the descriptions in IMP may not completely represent *bona fide* clinical practices in the Meiji era. Nevertheless, comparison of formulas from historical textbooks of pediatrics may uncover changes in pediatric Kampo. More generally, establishing a database of treatments from JKM classics is indispensable for revealing the

history of JKM.

In conclusion, based on the comparison of representative textbooks of pediatric Kampo, the current form of traditional pediatric Kampo may have developed less under the influence of traditional pediatrics developed before the abandonment of JKM in the late nineteenth century. A thorough investigation of pediatric books is needed to understand the history of pediatric Kampo.

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CONFLICT OF INTEREST

The author declares that there are no conflicts of interests to disclose.

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Figure 1. Breakdown of methods extracted from Yoyokasoku (In-house Methods of Pediatrics [IMP])

In all, 387 formulas (oral medications such as decoctions and powders) and 10 moxibustion/surgical treatments were extracted from the Methods section of IMP.

Fig. 1

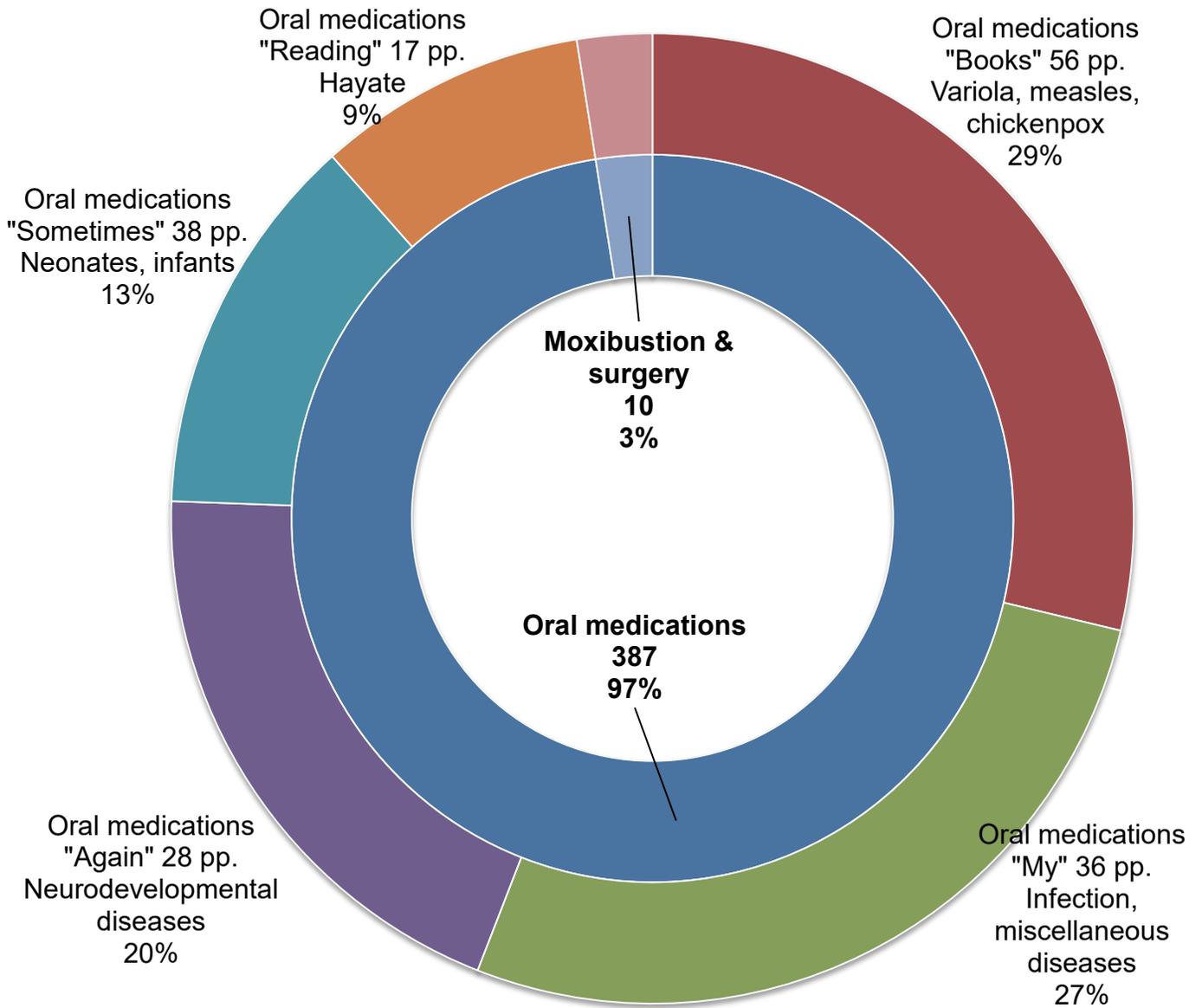


Figure 2. The classification of formulas in Yoyokasoku (In-house Methods of Pediatrics [IMP]) and ‘Shoni Kampo Chiryō no Tebiki’ (Manual of Pediatric Kampo Treatment [MPKT]).

Formulas were classified as classical formulas (red column), modern formulas (blue column), and Japanese originals (gray column), respectively. Each column is equivalent

to one formula. (a) Classification of formulas from IMP according to the disease clusters.

(b) Classification of formulas from the MPKT according to the disease clusters.

Fig. 2a

Volume	Disease clusters		Number of formulas			
Sometimes	初生雜病	Neonatal disease				
	五軟·五硬	Five stiffnesses/five flaccidities				
	變蒸	Growth fever				
	臍風·噁口	Umbilical wind/neonatal tetanus				
	大小便不通	Constipation/dysuria				
	鎖肛	Proctatresia				
	吐乳	Milk vomiting				
	腹痛	Abdominal pain				
Again	蟲積	Worm accumulation				
	驚風	Infantile convulsion				
	癲癇	Epilepsy				
	疳	Malnutrition				
	癆積	Hypochondriac accumulation				
	哺露, 丁奚	Infantile frequent vomiting, T-shaped malnutrition				
	疳眼, 雀目, 胎毒眼	Eye malnutrition, night blindness, fetal toxin eye				
	吃泥土	Pica				
	疳痢	Malnutrition dysentery				
	白濁淋	Cloudy strangury				
	淋	Strangury				
	語遲, 吃語	Language delay, stuttering				
	行遲, 齒遲, 髮遲	Moving, dental, hair growth retardation				
	解顛	Ununited skull				
	龜背, 龜胸	Tortoise back, tortoise chest				
	遺尿	Enuresis				
Reading	疝, 癪疝, 盤腸氣	Hernia, severe inguinal hernia, colon hernia				
My	早手	<i>Havate</i> (fulminant enterocolitis)				
	感冒, 傷寒	Common cold, cold damage				
	中寒	Cold stroke				
	中暑	Summer heat stroke				
	痢	Dysentery				
	咳嗽, 百啞嗽, 哮喘, 胎毒痰	Cough, neonatal cough, asthma				
	胎毒, 諸瘡	Fetal toxin, miscellaneous sore				
	丹毒	Erysipelas				
	口舌	Oral and tongue disease				
	頭瘡	Head sore				
	鼻	Nasal disease				
	聾耳, 耳聾	Impacted cerumen, deafness				
	Books	疥癬	Scabies			
痘疹		Variola				
麻疹		Measles				
	水痘	Chickenpox				

Japanese originals
 Modern formula
 Classical formula

Figure 3. Comparison of formulas from Japan's National Health Insurance (JNHI)-approved extracts, MPKT, and IMP.

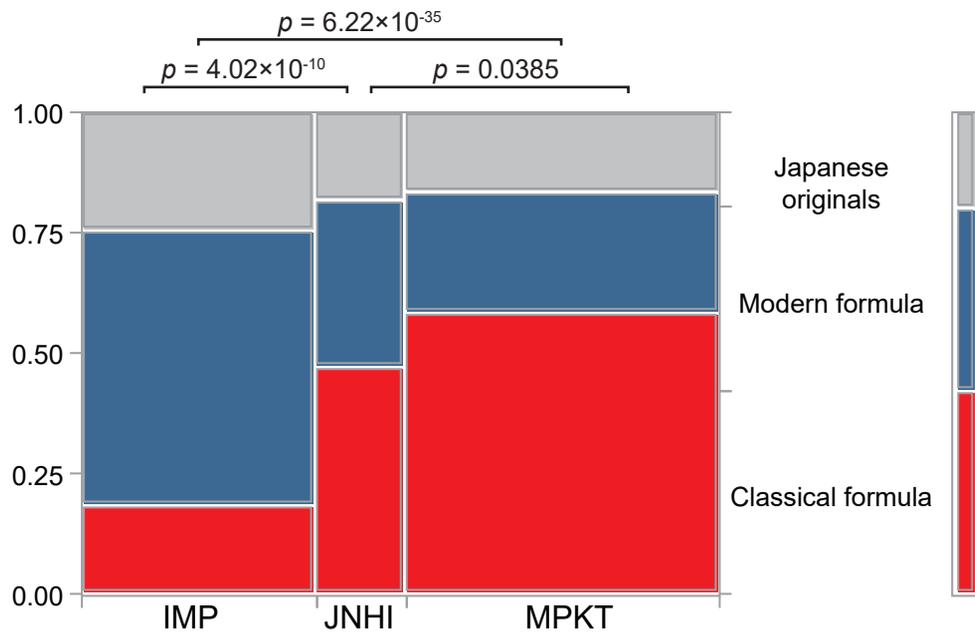
Left column shows classification of formulas from the IMP, middle from the JNHI-approved, and right from the MPKT. Statistical analysis was performed using Fisher's exact test.

Fig. 2b

Chapter	Disease clusters	Number of formulas									
1	Common cold, bronchitis	■	■	■	■	■	■	■	■	■	■
2	Influenza	■	■	■	■	■	■	■	■	■	■
3	Nasal obstruction, snoring, adenoiditis	■	■	■	■	■	■	■	■	■	■
4	Vomiting, diarrhea	■	■	■	■	■	■	■	■	■	■
5	Enterocolitis	■	■	■	■	■	■	■	■	■	■
6	Abdominal pain, constipation	■	■	■	■	■	■	■	■	■	■
7	Allergic disease	■	■	■	■	■	■	■	■	■	■
8	Bronchial asthma	■	■	■	■	■	■	■	■	■	■
9	Eczema, atopic dermatitis	■	■	■	■	■	■	■	■	■	■
10	Enuresis	■	■	■	■	■	■	■	■	■	■
11	Pediatric chronic glomerulonephritis, nephrotic syndrome	■	■	■	■	■	■	■	■	■	■
12	Edema, dehydration (heatstroke)	■	■	■	■	■	■	■	■	■	■
13	Orthostatic hypotension	■	■	■	■	■	■	■	■	■	■
14	Arrhythmia, cardiac disease	■	■	■	■	■	■	■	■	■	■
15	Night crying, tic, hypersensitivity, sleep disorder	■	■	■	■	■	■	■	■	■	■
16	Hyperventilation syndrome, seizure, epilepsy	■	■	■	■	■	■	■	■	■	■
17	Anorexia nervosa, eating disorder	■	■	■	■	■	■	■	■	■	■
18	School refusal, domestic violence, adjustment disorder	■	■	■	■	■	■	■	■	■	■
19	Autism spectrum disease, developmental disorder	■	■	■	■	■	■	■	■	■	■
20	Severe motor and intellectual disabilities	■	■	■	■	■	■	■	■	■	■
21	Frail children, frailty	■	■	■	■	■	■	■	■	■	■
22	Flabbiness, obesity, type II diabetes & dietary care	■	■	■	■	■	■	■	■	■	■
23	Hiesho (cold disorder)	■	■	■	■	■	■	■	■	■	■
24	Autoimmune disease	■	■	■	■	■	■	■	■	■	■
25	Pediatric hematology/oncology	■	■	■	■	■	■	■	■	■	■
26	Pediatric emergency medicine	■	■	■	■	■	■	■	■	■	■
27	Pediatric surgery	■	■	■	■	■	■	■	■	■	■
28	Adolescence	■	■	■	■	■	■	■	■	■	■

Japanese originals
 Modern formula
 Classical formula

Fig. 3



SUPPORTING INFORMATION

Table S1 List of all formulas from IMP.

Table S2 List of all formulas from MPKT.

Table S3 Disease names in common between IMP and MPKT, and the list of their formulas.