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Committee Report

The first nationwide survey of antimicrobial stewardship programs conducted by the Japanese Society of Chemotherapy☆

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1. Introduction

Antimicrobial stewardship (AMS) aims to improve the appropriateness of antimicrobial use to reduce resistance and benefit individual patients. Since the concept of AMS was first introduced in the 1970s [1], guidelines were issued in 2007 and 2016 by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) [2,3]. A previous meta-analysis reported that there were limited data on AMS in the Asia-Pacific region, including Japan [4]. In August 2017, the Japanese Society of Chemotherapy (JSC), along with the Japanese Association for Infectious Diseases, the Japanese Society for Infection Prevention and Control, the Japanese Society for Clinical Microbiology, the Pharmaceutical Society of Japan, the Japanese Society of Pharmaceutical Health Care and Sciences, the Japanese Society of Therapeutic Drug Monitoring, and the Japanese Society for Medical Mycology Joint Committee issued guidance for implementing antimicrobial stewardship programs (ASPs) to promote strategic and organizational aspects of AMS [5]. However, there are no national data regarding the implementation of ASPs in Japanese hospitals. Herein, we conducted a survey to clarify what percentage of hospitals nationwide is implementing ASPs and staffing resources. In order to gain a better understanding of these data, it is important to identify opportunities for improving ASP practices. The survey aimed to describe the

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strategies implemented and information regarding the main perceived barriers in Japan.

2. Materials and methods

2.1. Survey

An 18-question survey was developed by the JSC group on AMS based on JSC guidance [5] and the IDSA/SHEA guidelines (Supplementary material) [2,3].

The paper-based survey was distributed to certified members of the Japanese College of Infection Control Doctors (ICDs) on March 20, 2018, and survey responses were collected until April 23, 2018. The following were excluded: ministries and government offices, public health centers, nursing and home care facilities, industries, universities, institutes, and other centers of education and research. The cover letter asked the recipient to forward the survey to the hospital director and infection control practitioner. To avoid duplicates, one survey form was mailed per facility. The JSC covered the mailing expenses, and no incentives were provided for participation.

2.2. Statistical analysis

Survey results were analyzed using SPSS Statistics software version 23.0 (IBM Japan, Tokyo, Japan) with descriptive statistics to summarize responses. In summarizing the implementation of each ASP, hospitals that had not implemented hospital ASPs were excluded.

3. Results

3.1. Characteristics of respondents' facilities

A total of 1358 valid responses were received from 3532 providers, for an overall response rate of 38.4%. Table 1 presents the characteristics of respondents' facilities. Differences in characteristics between small/medium (≤300 beds) and large size hospitals (>300 beds) were observed. The small/medium size hospitals lacked on-site laboratories, AST organizations, number of pharmacists, and collaboration with ward pharmacists. Furthermore, less than half of hospitals with >500 beds had ASTs. ASPs were implemented in 67.9% (922/1358) of respondents' hospitals, particularly those with >20 beds (74.9%; 906/1206). The median (interquartile range) value of effectiveness of ASP activity in the respondents' facilities was 20 (0–50) (answer of Supplementary material Q8).

3.2. Implementation status of antimicrobial stewardship programs

The most frequently (>80%) implemented ASPs included monitoring antimicrobial consumption, appropriate specimen collection, registration system, therapeutic drug monitoring (TDM), and intervention for long-term use (Table 2), whereas the less frequently implemented ASPs included permission system, registration system with audit and feedback, antibiotic time-out, and interventions for special populations. As the hospital bed size increased, there was an increasing trend in the implementation rates of each ASP.

3.3. Human resources available for ASPs: existing and needed full-time equivalents (FTEs)

Fig. 1 shows the existing FTEs of each staff for ASPs and FTEs that respondents felt were needed to operate effectively. Very few existing FTEs of any staff were observed. A large gap in pharmacist FTEs between those existing (0–0.4) and needed (0.3–1.0) was observed for each bed size (Fig. 1B).

3.4. Essential and needed factors for enhancement of AMS

Fig. 2 shows the necessary factors that respondents think are effective for enhancing AMS in Japan. The most frequently needed resources were infectious disease (ID) pharmacists, resources of ID physicians, and health care fees for ASPs. Less than half (601/1343) of the facilities planned to bill for the revised additional reimbursement fee for infection prevention 2018 that newly approved the additional health care fee for ASPs.

4. Discussion

To the best of our knowledge, this is the first nationwide survey to report on the implementation of ASPs in Japan, including the FTEs of each health care worker. We revealed that two-thirds of

Table 1
Characteristics of respondents' facilities stratified by licensed bed size.

Characteristics	Total (n = 1358)	Licensed bed size				
		0–19 (n = 149)	20–100 (n = 145)	101–300 (n = 552)	301–500 (n = 320)	>500 (n = 192)
Additional reimbursement for infection prevention						
Type 1 + regional collaboration	665 (49.4)	2 (1.4)	7 (5.0)	213 (38.9)	260 (81.5)	183 (95.3)
Type 1	26 (1.9)	1 (0.7)	1 (0.7)	13 (2.4)	8 (2.5)	3 (1.6)
Type 2	403 (29.9)	1 (0.7)	80 (56.7)	280 (51.1)	37 (11.6)	5 (2.6)
None	253 (18.8)	143 (97.3)	53 (37.6)	42 (7.7)	14 (4.4)	1 (0.5)
Microbiology laboratory						
On-site laboratory	524 (39.0)	3 (2.0)	8 (5.6)	144 (26.5)	213 (67.0)	156 (81.3)
Branch laboratory or partial outsourcing	278 (20.7)	18 (12.2)	33 (23.1)	155 (28.5)	48 (15.1)	24 (12.5)
Outsourcing	542 (40.3)	127 (85.8)	102 (71.3)	244 (44.9)	57 (17.9)	12 (6.3)
Implementation of any ASPs, yes	922 (67.9)	16 (10.7)	60 (41.4)	376 (68.2)	283 (88.4)	187 (97.4)
AST organization						
AST with formal approval	198 (14.6)	0 (0)	2 (1.4)	55 (10.1)	61 (19.1)	80 (41.9)
Informal AST	41 (3.0)	0 (0)	1 (0.7)	12 (2.2)	17 (5.3)	11 (5.8)
ICT has been playing role of an AST	513 (37.9)	3 (2.0)	30 (20.7)	226 (41.3)	166 (51.9)	88 (46.1)
None	600 (44.4)	146 (98.0)	112 (77.2)	254 (46.4)	76 (23.8)	12 (6.3)
Collaboration with ward pharmacists, yes	613 (46.4)	3 (2.0)	39 (27.5)	236 (43.8)	195 (63.9)	140 (74.9)
Number of pharmacists per hospital pharmacy	13 (6–22)	0 (0–1)	3 (2–4)	8 (5–12)	18 (14–22)	37 (25–50)

ASPs, antimicrobial stewardship programs; AST, antimicrobial stewardship team; ICT, infection control team.
Data are presented as n (%) or median (interquartile range). Denominators differ for each question and represent the percentage of valid responses in each case.

Table 2
Implementation status of antimicrobial stewardship programs stratified by licensed bed size.

Characteristics	Total (n = 906)	Licensed bed size			
		20–100 (n = 59)	101–300 (n = 372)	301–500 (n = 279)	>500 (n = 186)
Prospective audit and feedback					
Specific antimicrobials	651 (72.7)	34 (57.6)	257 (69.1)	211 (75.6)	149 (80.1)
Specific infections or clinical conditions	447 (49.9)	20 (33.9)	149 (40.1)	150 (53.8)	128 (68.8)
Specific microorganisms	288 (32.1)	21 (35.6)	109 (29.3)	88 (31.5)	70 (37.6)
Others	4 (0.4)	1 (1.7)	1 (0.3)	0 (0.0)	2 (1.1)
None	114 (12.7)	13 (22.0)	61 (16.4)	33 (11.8)	7 (3.8)
Pre-authorization for specific antimicrobials					
Permission system	173 (19.2)	4 (6.7)	47 (12.6)	47 (16.7)	75 (40.1)
Registration system with audit and feedback	116 (12.8)	7 (11.7)	38 (10.2)	30 (10.6)	41 (21.9)
Registration system	763 (84.5)	50 (83.3)	319 (85.3)	246 (87.2)	148 (79.1)
None	17 (1.9)	3 (5.0)	10 (2.7)	3 (1.1)	1 (0.5)
Optimization for antimicrobial therapy					
De-escalation	594 (65.9)	24 (40.7)	194 (51.9)	219 (77.9)	157 (84.0)
Parenteral to oral conversion	278 (30.9)	12 (20.3)	80 (21.4)	94 (33.5)	92 (49.2)
TDM	743 (82.5)	33 (55.9)	286 (76.5)	251 (89.3)	173 (92.5)
Dose adjustment based on PK/PD parameters	569 (63.2)	28 (47.5)	206 (55.1)	185 (65.8)	150 (80.2)
Antibiotic time-out	52 (5.8)	6 (10.2)	14 (3.7)	17 (6.0)	15 (8.0)
Intervention for long-term use	734 (81.5)	40 (67.8)	288 (77.0)	243 (86.5)	163 (87.2)
Others	15 (1.7)	0 (0)	8 (2.1)	5 (1.8)	2 (1.1)
None	18 (2.0)	2 (3.4)	14 (3.7)	1 (0.4)	1 (0.5)
Diagnostic stewardship					
Gram stain	618 (69.0)	30 (53.6)	220 (59.0)	210 (74.5)	158 (85.4)
Appropriate specimen collection	759 (84.7)	44 (78.6)	299 (80.2)	246 (87.2)	170 (91.9)
Cascade or selective reporting	494 (55.1)	29 (51.8)	188 (50.4)	164 (58.2)	113 (61.1)
Point of care test	310 (34.6)	12 (21.4)	107 (28.7)	98 (34.8)	93 (50.3)
Hospital antibiograms	728 (81.3)	31 (55.4)	271 (72.7)	253 (89.7)	173 (93.5)
Biomarkers to start or stop antibiotics	459 (51.2)	20 (35.7)	179 (48.0)	150 (53.2)	110 (59.5)
Others	3 (0.3)	1 (1.8)	0 (0)	0 (0)	2 (1.1)
None	26 (2.9)	3 (5.4)	17 (4.6)	5 (1.8)	1 (0.5)
Measurement					
Monitoring of antimicrobial consumption	802 (89.4)	46 (78.0)	322 (86.8)	257 (91.8)	177 (94.7)
Monitoring of antimicrobial resistance	655 (73.0)	36 (61.0)	258 (69.5)	206 (73.6)	155 (82.9)
Process measurement of interventions	145 (16.2)	0 (0)	36 (9.7)	52 (18.6)	57 (30.5)
Outcome measurement of interventions	127 (14.2)	6 (10.2)	49 (13.2)	30 (10.7)	42 (22.5)
Others	1 (0.1)	0 (0)	0 (0)	1 (0.4)	0 (0)
None	61 (6.8)	10 (16.9)	28 (7.5)	16 (5.7)	7 (3.7)
Interventions for special populations					
Immunocompromised patients	68 (7.6)	2 (3.6)	20 (5.4)	23 (8.2)	23 (12.5)
Pediatrics and neonatology	41 (4.6)	4 (7.1)	10 (2.7)	12 (4.3)	15 (8.2)
Emergency department or intensive care unit	94 (10.6)	4 (7.1)	17 (4.6)	27 (9.6)	46 (25.0)
Invasive fungal infections	99 (11.1)	2 (3.6)	21 (5.7)	33 (11.7)	43 (23.4)
Others	10 (1.1)	1 (1.8)	4 (1.1)	4 (1.4)	1 (0.5)
None	702 (79.0)	48 (85.7)	319 (86.7)	220 (78.3)	115 (62.5)
Education					
Discussion with an attending physician	448 (49.8)	20 (33.9)	170 (45.6)	132 (47.0)	126 (67.7)
Lectures for hospital staff	464 (51.6)	28 (47.5)	163 (43.7)	144 (51.2)	129 (69.4)
Facility-specific guidelines development	571 (63.5)	34 (57.6)	219 (58.7)	177 (63.0)	141 (75.8)
Other	10 (1.1)	0 (0)	4 (1.1)	4 (1.4)	2 (1.1)
None	139 (15.5)	12 (20.3)	75 (20.1)	37 (13.2)	15 (8.1)

TDM, therapeutic drug monitoring; PK, pharmacokinetics; PD, pharmacodynamics.
Data are presented as n (%). Denominators differ for each question and represent the percentage of valid responses in each case. For hospitals with <20 beds, data were limited for implementation of antimicrobial stewardship programs.

respondents implemented any ASP as well as the percentage of each ASP implemented in Japanese hospitals. These findings provide useful benchmarks for those currently engaged in or planning to implement ASPs. ASP implementation estimates vary by country and region and are estimated to be 93.9% in Australia [6], 43.4% in France [6], 50.7% in the United States [7], and 58% according to the results of a worldwide cross-sectional survey [8]. Because the definition of ASPs in each study affects the implementation rates of ASPs, a coordinated international ASP survey is needed for comparison of clinical indicators.

In analyzing each ASP, registration system, TDM, monitoring of antimicrobial consumption, and monitoring of antimicrobial resistance were being implemented in many facilities regardless of bed size. These programs have been approved as requiring additional medical fee reimbursement [9]. Because the registration system has limited effect for restriction, its usefulness is said to be limited [5]. In Japan, few hospitals with ID physician resources have implemented antimicrobial permission systems such as preauthorization. JSC guidance has recommended for implementation of a registration system with audit and feedback instead of preauthorization in many facilities with limited ID physician resources [5].

IDSA guidelines have recommended both prospective audit and feedback (PAF) and preauthorization as core strategies of ASPs [2,3]. In the present survey, non-implementation rates for these programs were 12.7% and 1.9%, respectively. A recent study suggested that PAF was superior to preauthorization regarding appropriate antimicrobial use according to guidelines [10]. PAF should be a priority implementation program for interventions, but it generally depends on human and infrastructure resources for improving antibiotic use.

Although very few facilities implemented antibiotic time-outs, this is an important strategy to prompt prescribers to re-evaluate

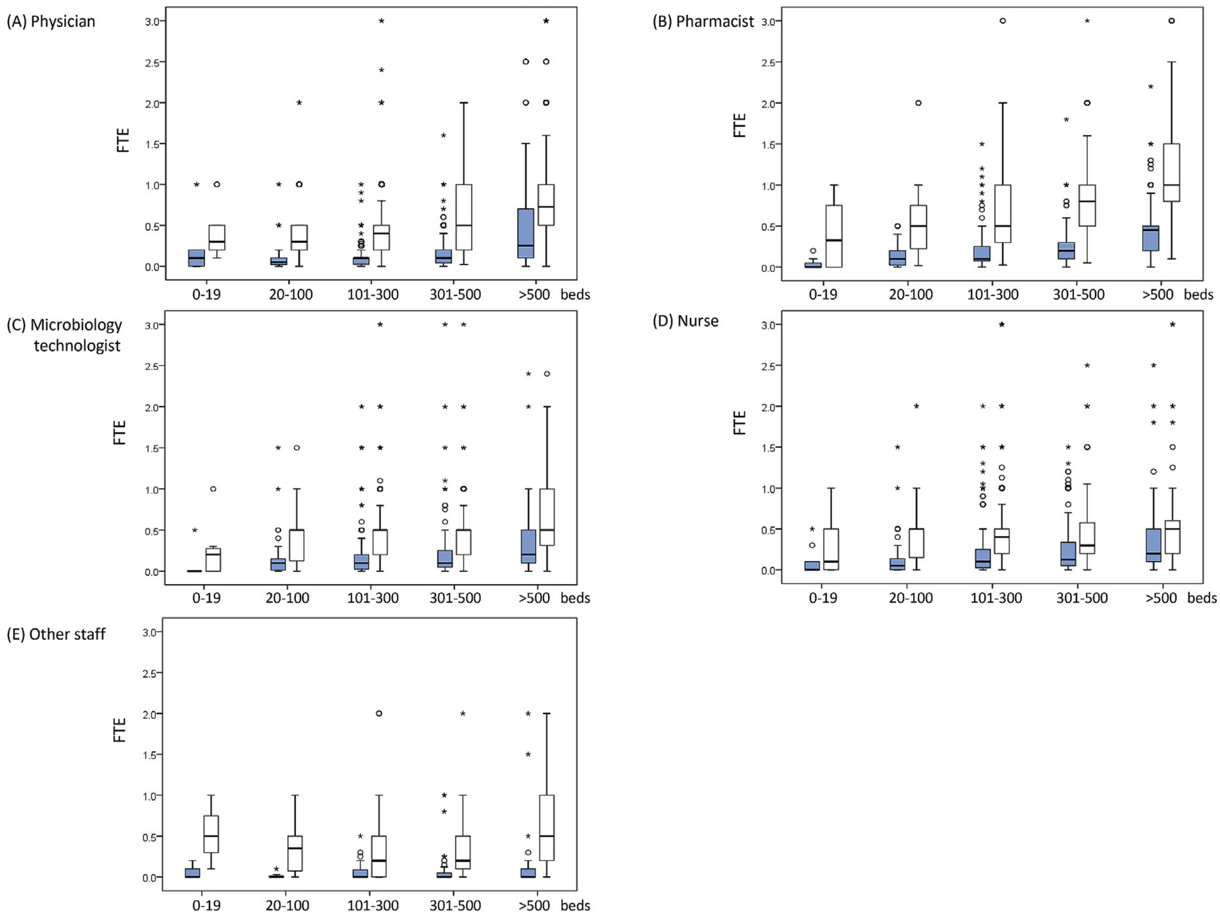

Fig. 1. Box plot ratios of full-time equivalents (FTEs) per occupied bed: existing and needed FTEs by (A) physician, (B) pharmacist, (C) microbiology technologist, (D) nurse, and (E) other staff. Gray bars = existing FTEs; white bars = needed FTEs.

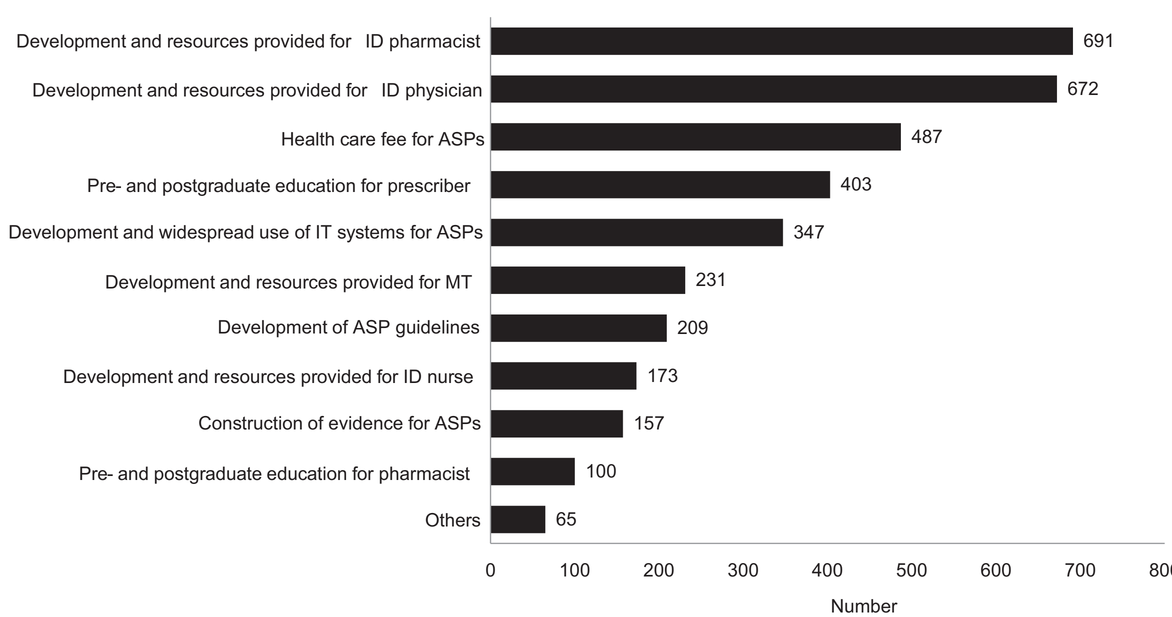

Fig. 2. Demand for enhancement of ASPs. Respondents were allowed to select a maximum of 3 answers for this question. ASPs, antimicrobial stewardship programs; IT, information technology; ID, infectious disease; MT, microbiology technologist.

Table 3
Requirements for additional reimbursement for infection prevention.

Structure
ICT in hospital, consisting of the following:
At least 1 infection control nurse with designed training and at least 1 physician, pharmacist and microbiology technologist with experience in infection control.
Type 1: physician or nurse with >0.8 FTE; the other with >0.5 FTE
Type 2: each member with >0.5 FTE
Practices
Distribution of hospital infection control policy to all wards
Educational lecture for all hospital staff
Ward audit/rounds and adherence monitoring of infection control practices (e.g. hand hygiene)
Collaboration with Type 1 and 2 facility regarding the infection control
Surveillance of antimicrobial consumption and hospital-associated infections
Implementation of antimicrobial stewardship programs (e.g. implementation of antimicrobial registration or permission system and intervention for long-term antimicrobial use)

ICT, infection control team; FTE, full-time equivalent.

antibiotic appropriateness, including the need for de-escalation and discontinuation [11]. However, previous studies reported a low implementation rate for automatic stop order strategies [8,12]. IDSA guidelines suggest that limited data confirm the feasibility or sustainability of these systematic prescriber-led review strategies (e.g., antibiotic time-out, automatic stop order) [3].

The results of our survey demonstrate the current lack of staff FTEs for ASPs in most Japanese hospitals as well as the value of effectiveness of ASP activity that respondents felt was present in their facility. It is critical to provide human resources based on the volume of the organization and implement any effective programs. The IDSA task force reported that existing FTEs of both pharmacists and physicians in the United States were 0.61–1.5 and 0.27–0.46, respectively [13]. Moreover, the IDSA recommended FTE support of 1.0–3.0 in pharmacists and 0.4–1.0 in physicians according to bed size. FTE support is essential for successful ASPs and does not replace other resources such as IT systems. A recent study by the Centers for Disease Control and Prevention (CDC) found an association between salary support and an organization's ability to have a comprehensive ASP [14]. Moreover, a recent IDSA survey reported an independent relationship between physician and pharmacist FTE and effectiveness of ASPs [13]. We believe that the lack of manpower has been the main barrier of AMS in Japan.

In our survey, most respondents felt that ASPs were understaffed, and many respondents desired additional FTE support; in particular, there was a high demand for both pharmacists and physicians. These results reinforce the integral role of both the pharmacist and physician in effective implementation of ASPs. A stronger commitment to health care policy may be needed to develop human resources for both pharmacists and physicians, and it is also important to develop ID-trained pharmacists and ID physicians with leadership skills geared toward improving the use of antimicrobials supported by the JSC.

The limitations of this research include reliance on a self-reported survey; whether this reflects true implementation is unclear as we did not inquire about the quality and quantity of ASPs. The survey was designed to inquire about AMS practices. Moreover, we did not inquire about the outcomes of interventions such as effect on antimicrobial consumption and rates of multidrug-resistant organisms. Further surveys are needed as the implementation of ASPs progresses in Japan. In addition, it is not known whether the facilities without ICD implemented ASPs. However, respondents for facilities with ≥20 beds covered 14.4% (1209/8389) of Japanese hospitals with ≥20 beds as of March 31, 2018 [15]. Thus, we believe that our survey reflects hospital AMS of various sizes and types nationwide. Finally, further analyses are needed to develop a reasonable FTE for each staff according to bed size [16]. Future developments of a proposed FTE-to-bed ratio will be required in Japan.

Since an additional reimbursement of 4000 yen (type 1) and 1000 yen (type 2) per patient per admission was introduced according to infection prevention activity in each hospital in 2012 [17], the implementation of ASPs was enhanced in these hospitals (Table 3). The revised additional reimbursement fee for infection prevention 2018 in Japan was approved as an additional health care fee for ASPs. This health policy will help drive the implementation of comprehensive ASPs in Japan. Repeating this survey in the future will help monitor the effect of health policy.

In summary, we reported data on ASPs and staffing resources, which can be used by Japanese hospitals to start and sustain ASPs. This would be a reasonable starting activity for ASPs or those needing to prioritize.

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Conflicts of interest

Masafumi Seki received speaker honoraria from Astellas Pharma, Inc., Dainippon Sumitomo Pharma Co., Ltd., Daiichi Sankyou Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Meiji Seika Pharma Co., Ltd., MSD Japan, Pfizer Japan, Inc., research grants from Astellas Pharma Inc., Nippon Boehringer Ingelheim Co., Ltd., Daiichi Sankyou Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Meiji Seika Pharma Co., Ltd., MSD K.K., Shionogi & Co., Ltd.

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Appendix A. Supplementary data

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