

# Non-drug and surgical treatment algorithm and recommendations for the 2020 update of the Japan College of Rheumatology clinical practice guidelines for the management of rheumatoid arthritis—secondary publication

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# ABSTRACT

**Objectives:** The aim of this study was to update the Japan College of Rheumatology (JCR) clinical practice guidelines (CPGs) for the management of rheumatoid arthritis (RA) and prepare an algorithm for non-drug and surgical treatments. This article is a digest version of the guidelines.

**Methods:** The Japanese Ministry of Health, Labour and Welfare's research group, in collaboration with the JCR, used the Grading of Recommendations, Assessment, Development, and Evaluation method to update the 2014 JCR CPG for RA. The consensus was formed by CPG panel members.

**Results:** We raised 19 clinical questions regarding non-drug and surgical treatments for RA and developed recommendations. The treatments included exercise therapy; occupational therapy; joint injection of corticosteroids; and orthopaedic surgeries including cervical spine surgery, wrist and foot arthroplasty, ankle arthrodesis, and replacement arthroplasty of the shoulder, elbow, finger, hip, knee, and ankle. Recommendations regarding the risks of surgery and perioperative discontinuation of medications have also been developed. Based on these recommendations, we created an original algorithm for the non-drug and surgical treatment of RA.

**Conclusions:** These recommendations are expected to serve rheumatologists, health care professionals, and patients with RA as tools for shared decision-making to treat residual limb joint symptoms and functional impairment.

KEYWORDS: Clinical practice guideline; non-drug treatment; rheumatoid arthritis; surgical treatment; systematic review

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## Introduction

Highly effective medications, such as biological diseasemodifying antirheumatic drugs (bDMARDs), have decisively brought about a paradigm shift in the treatment of rheumatoid arthritis (RA) in Japan [1, 2]. However, more than 30% of patients still have moderate or high disease activity [1, 2]. Some of these patients, and even those in remission, sometimes require orthopaedic surgical intervention [3, 4]. Moreover, many patients require additional nondrug treatments, such as exercise, occupational therapy, intra-articular injection, or surgical treatment to supplement drug treatment, as exemplified by a recently published report [5].

Many recommendations and guidelines have been regularly published to support clinicians, health care professionals, and patients, but most focus on drug treatments. The recently published recommendations by the American College of Rheumatology dedicated some part to non-drug treatment options [6], but no comment was made regarding surgical treatment. In contrast, the first published guidelines for managing patients with RA in Japan included recommendations for surgical treatment in 2004 [7].

Furthermore, non-drug and surgical treatments were included in the clinical practice guidelines (CPG) for the management of RA in Japan, published by the Japan College of Rheumatology (JCR) in 2014 [8]. However, some crucial surgeries were not commented upon in the guidelines, and the treatment options for RA have undergone further modifications with the approval of new drugs and advances in surgical and rehabilitation treatments. Moreover, an algorithm for these treatments has never been published and is eagerly requested by rheumatologists and healthcare professionals to recommend treatments for patients who desire further functional improvement in daily life. To respond to these needs, we have revised the non-drug and surgical treatments in the 2014 CPG, added a few recommendations, and newly developed an algorithm for these treatments. This article outlines the recommendations for non-drug and surgical treatments in the 2020 CPG for managing RA and the treatment algorithm developed based on these recommendations.

## **Materials and methods**

## CPG development process

The Organization for the Development of Guidelines was formed by a subcommittee on guidelines for the management of RA of the Clinical Epidemiological Study for the Standardization of Treatment for Rheumatoid Arthritis in Japan, which was supported by a Ministry of Health, Labour, and Welfare Policy Research Grant (Research on Immunologic and Allergic Disease). The development of this guideline followed the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system (GRADE Working Group. http://www.gradeworkinggroup.org/). A total of 18 members of the systematic review (SR) group and 18 members of the CPG group drafted the recommendations. The results of a patient questionnaire survey [9] and opinions of patient representatives were also considered. After thorough and repeated discussions, the CPG development group (CPG panel) and three patient representatives (Japan Rheumatism Friendship Association) reached a consensus on the recommendations.

# Important clinical questions regarding non-drug and surgical treatments

The important clinical questions (CQ) for non-drug and surgical treatments in the 2020 CPG were first provided by four CPG members, who were orthopaedic surgeons. The steering committee decided on these questions, and each CQ regarding patients, interventions/exposures, comparators, and outcomes (PICO/PECO, respectively) was prepared by the CPG panel. Some surgical results did not include comparators. In such cases, the preoperative and postoperative scores were compared. Next, each pair of CPG panel members determined keywords and search formulae for each CQ and requested the Japan Medical Library Association to search PubMed, the Cochrane Library, and Japana Centra Revuo Medicina databases. Manual searching was performed when necessary.

Since the literature search period used to prepare the 2014 CPG was from 2005 to August 2012, the search period for the 2020 CPG was set to be from September 2012 to September 2019. Because of the scarcity of evidence on orthopaedic surgeries, some COs required an extended period to facilitate the collection of sufficient literature. The study designs included randomised controlled trials (RCTs), longitudinal cohort and registry studies, and cross-sectional studies. The identified articles were divided into those for quantitative meta-analysis (SR articles) and those for others. One of the two investigators in charge of each CO read the title, abstract, and, if necessary, the full text of the article to examine whether it matched the PECO/PICO of the CQ, while the second investigator checked the process and results. We described the search process in a flowchart and recorded the reasons for the exclusion of articles (ESM Figure S1).

# Systematic review

We selected seven or fewer critical outcomes to make recommendations according to the recommendations of the GRADE Working Group. Critical outcomes selected for nondrug and surgical treatments included survivorship of joint replacement or other orthopaedic surgeries, postoperative patient-reported outcomes (PROs), such as pain and health assessment questionnaires (HAQ), clinical scores for the joint indicated, postoperative complications, scores for structural damage of joints, and composite measures, such as the disease activity score-28 (DAS28) and Simple Disease Activity Index. For CQ#51, we selected a separate set of critical outcomes, including orthopaedic surgery, joint replacement, knee joint replacement, large joint replacement, and wrist surgery. Because of the scarcity of evidence in some CQs, we selected substitutional, important outcomes to develop recommendations. Next, using the GRADE method, the investigator in charge of each CO assessed the certainty of the evidence for each critical outcome (ESM Table S1), followed by an assessment of the overall outcomes (i.e. overall quality of evidence), based on the study design and eight grading factors.

Recommendations were prepared by considering the following factors: (1) overall quality of evidence, (2) balance of desirable and undesirable consequences, (3) patients' values and preferences, and (4) costs and available resources. The direction of recommendation was 'recommend' or 'do not recommend' (for/against), and the strength was rated as 'strong' or 'weak (conditional).' In the modified Delphi voting by the CPG panel members and three patient representatives, a score of 7 or more on a scale of 1 to 9 was used as the criterion for agreement with a recommendation presented by an investigator in charge. The agreement was considered to have been reached when 70% or more of the participants agreed in the first vote and two-thirds or more in the second and third votes. A total of 19 non-drug and surgical treatment recommendations were finalised after the CPG panel discussion. The related literature for CQ 51 was summarised and published elsewhere [10].

All statistical analyses were conducted using Review Manager, version 5.4.1. (Cochrane Collaboration: Review Manager, RevMan version 5.3.5; The Nordic Cochrane Center, The Cochrane Collaboration, 2014, Copenhagen, Denmark). We also used the GRADEpro GDT software (https://gradepro.org/) to build evidence profiles (certainty assessment and summary of findings).

# Results

The 2020 CPG was officially published as a guideline of the JCR after an evaluation by the evidence-based medicine promotion project (Minds) of the Japan Council for Quality Health Care, and a request for public comments from the JCR, the Pediatric Rheumatology Association of Japan, and the Japanese Orthopedic Association [11]. The Appraisal of Guidelines for Research & Evaluation (AGREE) II was used for the evaluation by Minds. The algorithm and recommendations for non-drug and surgical treatments are summarised in Table 1 and below, supplemented by the evidence profiles (ESM Table S2).

# Non-drug and surgical treatment algorithm (Figure 1)

This algorithm was suggested by orthopaedic surgeons who were members of the CPG and approved by all members of the CPG after careful discussions. First, non-drug and surgical treatments must be considered only after sufficient and intensive drug treatment had been conducted because an SR of these guidelines shows that early and efficacious drug treatment can decrease the incidence rates of orthopaedic operations in patients with RA (Recommendation 51) [12, 13]. Second, the algorithm should be applied to patients with chronic joint disabilities. Situations that should be excluded from this algorithm include acute conditions, such as fracture, infection, myelopathy, tendon rupture, or other conditions that require urgent surgical or non-surgical treatment.

# Phases I and II

In Phase I, after continuous and intensive drug treatment, the patients are carefully evaluated by rheumatologists and healthcare professionals to determine whether residual limb joint symptoms or functional impairment remain. If any of those remains, the causes and degrees of, or possible treatment options against the symptoms or impairment are assessed and discussed. A significant proportion of these patients may require referral to physical or occupational therapists or orthopaedic surgeons. Non-drug treatment includes rehabilitation, intra-articular corticosteroid injection, and orthosis (Recommendations 52, 53, and 54). Lifestyle guidance is also recommended. When these treatments are successful, their continuation is suggested until they are no longer necessary. The patient then continuously follows the algorithm and recommendations for drug treatment. However, if non-drug treatment is considered ineffective or insufficient, the treatment proceeds to Phase II. Adequate timing is crucial in consideration of proceeding to Phase II.

In Phase II, residual joint symptoms or functional impairment were carefully re-evaluated. If residual functional disabilities or deformities are considered severe, or the limited number of arthritic joints is considered refractory to drug treatment, the possibility of reconstructive joint surgery is considered. When it is suspected that the surgery will cause insufficient improvement or when the demerits outweigh the potential merits of the operation, surgical treatment is not suitable, and non-surgical treatment is continued.

The patients' preference for surgical treatment and necessary support after surgery is carefully assessed. If orthopaedic surgical treatment is indicated, careful assessment of surgical options is required. Orthopaedic surgical interventions may include artificial joint replacement, joint-preserving arthroplasty, arthrodesis, or synovectomy depending on the joint and the degree of destruction in consideration, but artificial joint replacement or joint-preserving arthroplasty are prioritised if available. After surgery, continuous rehabilitation treatment is considered to improve or maintain functional recovery. Drug treatment is continued at any point or during any course of non-drug or surgical treatment.

# Recommendations for non-drug and surgical treatments (Table 1)

## Orthopaedic surgical treatments

Surgical options are available for most limb joints and spines when conservative treatments are ineffective or show inadequate response. In particular, large joints can undergo effective total joint arthroplasty (artificial joint replacement), except for the wrist, for which there are no currently reliable implants. However, it is unclear when, which, and to what extent surgical options should be considered in patients with RA. Therefore, we first raised a group of CQs regarding the efficacy of the respective orthopaedic operations in patients with RA (Table 2). These CQs are addressed in the recommendations for the cervical spine (Recommendation 50) [14], total joint arthroplasty of the shoulder (Recommendation 42) [15], elbow (Recommendation 39) [16], finger (Recommendation 41) [17], hip (Recommendation 44) [18, 19], and knee (Recommendation 46) [20, 21], and wrist joint arthroplasty (except total wrist arthroplasty; Recommendation 40) [22]. The evidence for total wrist arthroplasty was considered insufficient for patients with RA at the time of the SR, and we did not create a CQ for this treatment. The CPG panel strongly recommended total joint arthroplasty of the knee and hip and weakly (conditionally) recommended arthroplasty of the other joints. The second group of CQs compared the two surgical options for an impaired joint (Table 2). These CQs are addressed in the recommendations for the comparison of (anatomical) total shoulder arthroplasty and hemiarthroplasty (Recommendation 43), cemented and cementless total hip replacement (Recommendation 45), total ankle arthroplasty and arthrodesis (Recommendation 47), and resection arthroplasty and joint-preserving operation of the toes (Recommendation 49). Although some differences existed, each comparison showed similar outcomes [15, 23-25], and

## Table 1. CQ and recommendations.

| No <sup>a</sup> | Clinical question  | Recommendation  | Strength of recommendation | Certainty of evidence |
|-----------------|--|---|----------------------------|-----------------------|
| 37              | Is it necessary to discontinue MTX during<br>the perioperative period of orthopaedic   | We suggest not discontinuing MTX during<br>the perioperative period of orthopaedic  | Weak                       | D (very low)          |
| 38              | Is it necessary to discontinue bDMARD<br>during the perioperative period of<br>orthopaedic surgery?  | We suggest discontinuing bDMARD<br>during the perioperative period of<br>orthopaedic surgery.   | weak                       | D (very low)          |
| 39              | Is total elbow arthroplasty useful for<br>managing RA?   | We suggest total elbow arthroplasty for<br>functional disability of the elbow joint<br>with structural damage in patients with<br>RA.   | Weak                       | D (very low)          |
| 40              | Is wrist joint arthroplasty (except for total<br>wrist arthroplasty) useful for managing<br>RA?  | We suggest partial wrist arthrodesis of<br>the radio-carpal joint and the Sauvé–<br>Kapandji procedure for the destruction of<br>the wrist joint in patients with RA.   | Weak                       | D (very low)          |
| 41              | Is finger joint arthroplasty useful for managing RA?   | We suggest silicone metacarpophalangeal<br>joint arthroplasty for the destruction<br>of the metacarpophalangeal joints in<br>patients with RA.  | Weak                       | D (very low)          |
| 42              | Is total shoulder arthroplasty useful for managing RA?   | We suggest total shoulder arthroplasty for<br>the functional disability of the shoulder<br>joint with structural damage in patients<br>with RA.   | Weak                       | D (very low)          |
| 43              | Is total shoulder arthroplasty more useful<br>than hemiarthroplasty for shoulder joint<br>disorders for managing RA?   | We suggest both total shoulder arthro-<br>plasty and hemiarthroplasty for the<br>destruction of the shoulder joint with<br>functional disability in patients with RA.   | Weak                       | D (very low)          |
| 44              | Is total hip arthroplasty useful for managing RA?  | We recommend total hip arthroplasty for<br>functional disability of the hip joint with<br>structural damage in patients with RA   | Strong                     | D (very low)          |
| 45              | Is cementless total hip arthroplasty as use-<br>ful as cemented total hip arthroplasty for<br>hip joint disorders for managing RA2   | We suggest both cemented and cement-<br>less total hip arthroplasty for hip joint<br>disorders in patients with RA  | Weak                       | D (very low)          |
| 46              | Is total knee arthroplasty useful for<br>managing RA?  | We recommend total knee arthroplasty<br>for functional disability of the knee joint<br>with structural damage in patients with<br>RA.   | Strong                     | D (very low)          |
| 47              | Is total ankle arthroplasty more useful than ankle arthrodesis for managing RA?  | We suggest both total ankle arthroplasty<br>and ankle arthrodesis for functional dis-<br>ability of the ankle joint with structural<br>damage in patients with RA.  | Weak                       | D (very low)          |
| 48              | Do incident rates of surgical site infection,<br>delayed wound healing, and postoper-<br>ative death increase when orthopaedic<br>surgery is performed in RA patients with<br>comorbidities? | When orthopaedic surgery is performed in<br>RA patients with comorbidities, incident<br>rates of surgical site infection, delayed<br>wound healing, and postoperative death<br>can increase. We recommend careful<br>observation and treatment for those<br>patients. | Strong                     | C (low)               |
| 49              | Is joint-preserving surgery of the toes more<br>useful than resection arthroplasty for<br>managing RA?   | We suggest joint-preserving operation<br>and resection arthroplasty of the toes<br>for functional disability of the toes with<br>structural damage in patients with RA  | Weak                       | D (very low)          |
| 50              | Is cervical operation useful for cervical myelopathy for managing RA?  | We suggest cervical operation for cervical<br>myelopathy in patients with RA before<br>neurological symptoms become severe<br>and subluxation becomes irreducible.  | Weak                       | D (very low)          |
| 51              | Does drug treatment decrease incident<br>rates of orthopaedic operations in RA<br>patients with risk factors for future<br>orthopaedic surgery?  | We suggest early and efficacious drug<br>treatment to decrease incident rates<br>of orthopaedic operations in patients<br>with RA and risk factors for future<br>orthopaedic surgery.   | Weak                       | D (very low)          |
| 52              | Does exercise therapy improve PROs for   | We recommend exercise therapy for improving PROs in particular with $PA$  | Strong                     | B (moderate)          |
| 53              | Does occupational therapy improve PROs for managing RA?  | We recommend occupational therapy for<br>improving PROs in patients with RA.  | Strong                     | D (very low)          |

(continued)

#### Table 1. (Continued)

| No <sup>a</sup> | Clinical question   | Recommendation   | Strength of recommendation | Certainty of evidence |
|-----------------|---|--|----------------------------|-----------------------|
| 54              | Does glucocorticoid intra-articular<br>injection improve PROs for managing<br>RA? | We suggest glucocorticoid intra-articular<br>injection for improving PROs in patients<br>with RA. We should perform it in a short<br>period under sufficient drug therapy.       | Weak                       | D (very low)          |
| 55              | Does joint surgery improve PROs for<br>managing RA?                               | We suggest joint surgery for improving<br>PROs in patients with RA. Joint surgery<br>should be performed at proper tim-<br>ing and with careful physical function<br>evaluation. | Weak                       | D (very low)          |

<sup>a</sup>Please note that the recommended numbers range from 37. Recommendations 1–36 are for the drug treatments of RA.



Figure 1. Non-drug and surgical treatment algorithm for 2020 JCR CPG for the management of RA.

\*1: Excludes acute conditions such as fracture, infection, myelopathy, tendon rupture, or other conditions requiring urgent surgery.

\*2: Includes orthosis and lifestyle guidance.

\*3: The appropriate timing of surgery is crucial.

\*4: Unsuitable for surgery when the surgery brings only insufficient improvement or when the demerit outweighs its merit. Consider the patient's preferences and

- necessary support after surgery.
- \*5: Prioritise joint replacement and joint-preserving arthroplasty if available.
- \*6: Consider adequate drug treatment during or after surgery and rehabilitation.

the CPG panel weakly (conditionally) recommended both surgical treatments for the four CQs. The third group of CQ was about the changes in PROs by orthopaedic surgical treatment (Table 2) and led to Recommendation 55 [26–28]. The surgical procedures were divided into upper and lower limb surgeries, and both showed statistically significant improvement in PROs in the meta-analysis.

Notably, the overall quality of evidence was very low in all of the recommendations. However, the panel unanimously recommended each of these treatments.

## Exercise and occupational therapies

We raised CQs on whether rehabilitation treatment can improve PROs in patients with RA (Recommendations 52 and 53). The collected evidence was divided into exercise and occupational therapies. An SR and meta-analysis showed that exercise and occupational therapies could improve composite measures and PROs [29–31]. The overall quality of evidence was moderate for exercise and very low for occupational therapy. The CPG panel strongly recommended exercise therapy. Considering the balance of desirable and undesirable consequences, patients' strong values and preferences, and a high level of agreement, the CPG panel also strongly recommended occupational therapy to improve PROs, despite the lower level of collected evidence for its efficacy than exercise therapy.

#### Intra-articular corticosteroid injection

Intra-articular injection of corticosteroids is one of the most effective treatments for residual joint symptoms in patients with RA. We revised the recommendations in the 2014 CPG and rewrote the CQ to determine whether this treatment could improve PROs in patients with RA (Recommendation 54). Collected evidence and meta-analysis show that the injection can improve PROs, such as HAQ-DI and pain, in both the knee and wrist [32]. The overall quality of evidence was very low. The CPG weakly (conditionally) recommended intra-articular injection to improve PROs on the premise of sufficient drug treatment, and it should be used only for the short term.

| Table 2. Groups of | <sup>-</sup> CQ raised in | non-drug and | surgical | treatment. |
|--------------------|---------------------------|--------------|----------|------------|
|--------------------|---------------------------|--------------|----------|------------|

| Groups of clinical question  | Clinical question  | CQ number |
|--|--|-----------|
| Does drug treatment affect future incident rates of orthopaedic surgery?     | Does drug treatment decrease incident rates of orthopaedic operations<br>in RA patients with risk factors for future orthopaedic surgery?  | 51        |
| Is orthopaedic surgery useful for managing RA?                               | Is cervical surgery useful for cervical myelopathy for managing RA?  | 50        |
|  | Is total shoulder arthroplasty useful for managing RA?   | 42        |
|  | Is total elbow arthroplasty useful for managing RA?  | 39        |
|  | Is finger joint arthroplasty useful for managing RA?   | 41        |
|  | Is total hip arthroplasty useful for managing RA?  | 44        |
|  | Is total knee arthroplasty useful for managing RA?   | 46        |
|  | Is wrist joint arthroplasty (except for total wrist arthroplasty) useful for managing RA?  | 40        |
| Which surgical option is more useful for managing RA?                        | Is total shoulder arthroplasty more useful than hemiarthroplasty for shoulder joint disorders for managing RA?   | 43        |
| 0.0  | Is cementless total hip arthroplasty as useful as cemented total hip arthroplasty for hip joint disorders for managing RA?   | 45        |
|  | Is total ankle arthroplasty more useful than ankle arthrodesis for managing RA?  | 47        |
|  | Is joint-preserving surgery of the toes more useful than resection arthroplasty for managing RA?   | 49        |
| Does non-drug and surgical treatment improve PROs for managing RA?           | Does exercise therapy improve PROs for managing RA?  | 52        |
| 1 00   | Does occupational therapy improve PROs for managing RA?  | 53        |
|  | Does glucocorticoid intra-articular injection improve PROs for<br>managing RA?   | 54        |
|  | Does joint surgery improve PROs for managing RA?   | 55        |
| How should drug treatment be managed perioperatively?                        | Is it necessary to discontinue MTX during the perioperative period of orthopaedic surgery?   | 37        |
|  | Is it necessary to discontinue bDMARD during the perioperative period<br>of orthopaedic surgery?   | 38        |
| How do comorbidities affect perioperative complications in patients with RA? | Do incident rates of surgical site infection, delayed wound healing, and<br>postoperative death increase when orthopaedic surgery is performed<br>in RA patients with comorbidities? | 48        |

### Perioperative risks of surgical intervention

One of the most important factors when considering surgical treatment of RA is the perioperative risk of complications. In the 2014 CPG, we provided recommendations on the risks of surgical site infection and delayed wound healing caused by bDMARDs; however, in the 2020 CPG, we decided to raise a broader question on the risks associated with surgical treatment: 'Do incident rates of surgical site infection, delayed wound healing, and postoperative death increase when orthopaedic surgery is performed in RA patients with comorbidities?' (Recommendation 48). The evidence was collected from observational studies and did not include RCTs. It showed an increased risk of adverse outcomes in RA patients with comorbidities such as obesity, diabetes mellitus, chronic obstructive pulmonary disease, and ischaemic heart disease. The overall quality of the evidence was low. The CPG panel strongly recommended careful observation and treatment of RA patients with comorbidities undergoing surgical treatment because the incidence rates of surgical site infection, delayed wound healing, and postoperative death may be increased [33]. An associated SR has been published elsewhere [10].

### Perioperative discontinuation of RA medications

The extent of the use of drugs in the perioperative period has been debatable since the introduction of effective and immunologically potent treatments. We again raised whether it is necessary to discontinue methotrexate (MTX) or bDMARDs during the perioperative period of orthopaedic surgery (Recommendations 37 and 38). Two RCTs and four observational comparative studies on MTX showed that its continuation suppressed the risk of flare-up and did not affect the risk of surgical site infection or delayed wound healing.

In contrast, two SRs and seven observational comparative studies regarding bDMARDs showed that the continuation of perioperative use of bDMARDs might increase the risk of SSI and delayed wound healing. The evidence collected was limited; however, based on other recommendations and guidelines and our systematic review, we weakly (conditionally) recommend continuing MTX and discontinuing bDMARDs during the perioperative period of orthopaedic surgery [34]. However, the evidence is insufficient, and studies on the discontinuation period have rarely been reported.

## Discussion

Because medical infrastructure and treatment options in Japan differ in many aspects from those in other countries, this 2020 CPG was developed for patients and medical professionals in Japan through the method recommended by the GRADE system. We developed recommendations and an algorithm for non-drug and surgical treatments. To the best of our knowledge, this is the first algorithm published in English for nondrug and surgical treatments for RA. Moreover, the algorithm for non-drug and surgical treatments was designed to complement the one for drug treatment, which is a unique and robust feature of this algorithm. However, good quality evidence for the efficacy of non-drug and surgical RA treatments is scarce, and the overall quality of evidence of the recommendations is mostly very low. Rheumatologists, healthcare professionals, and patients who refer to these recommendations should always take this into consideration.

One of the strengths of this CPG is that the recommendations are supported by patients. Three patient representatives participated in the discussion, provided their opinions even on non-drug and surgical treatments, and voted for recommendations. Furthermore, we conducted a questionnaire survey of patients with RA before developing recommendations, with responses from 1156 patients (response rate: 72.3%) [9]. Almost 90% of patients were satisfied with joint replacement arthroplasty of the hip and knee 15 years postoperatively. These results strongly support the recommendations for non-drug and surgical treatment in the 2020 CPG.

Another strength of the 2020 CPG is that the recommendations were developed through careful and repeated discussions among various medical professionals, including rheumatologists, paediatric rheumatologists, orthopaedic surgeons, and guideline specialists. Of note, orthopaedic surgeons who are either very familiar with or experts in drug and rehabilitation treatments for RA also treat patients with the disease in Japan [35]. This unmatched medical environment made a unique CPG panel possible. From a comprehensive perspective, the recommendations suggested in the 2020 CPG can provide helpful treatment options for patients in Japan and other countries.

As described earlier, the evidence for the efficacy of nondrug and surgical treatments is quite limited, and recommendations are supported by low-quality evidence compared with that for drug treatment. From a practical or ethical perspective, most surgical treatments cannot be compared in RCTs; a high level of evidence should always be pursued while planning clinical studies, but a different system to assess the evidence for non-drug and surgical treatments is strongly awaited. This discussion should be continued in the future.

Another point of consideration is that we had to omit several non-drug and surgical treatment options from the 2020 CPG, although these were considered useful in selected circumstances. For example, orthosis, many non-artificial joint operations such as synovectomy, and spinal operations for pain and disabilities due to spinal deformities were omitted, but they are frequently dealt with in many medical and practical situations. These treatment options should be discussed and added to future CPGs.

The primary purpose of developing a CPG is to provide recommendations based on recent evidence and thorough discussions among stakeholders and to help facilitate a shared decision-making process between patients and medical professionals. To this end, we developed a previously unpublished algorithm for non-drug and surgical treatments. Although the recommendations and algorithm can support most patients, this CPG is unsuitable for some patient groups. The reasons include differences in patients' backgrounds and medical environments, the divergence of patient preferences, and vast discrepancies in the patients' financial situations. Therefore, patients must not be forced to comply with recommendations or algorithms, and personal expectations and decisions should be respected. All rheumatologists and healthcare professionals should bear this in mind and support informed decision-making by individual patients.

In conclusion, the 2020 CPG's treatment algorithm and non-drug and surgical treatment recommendations were developed by a research group of the Japanese Ministry of Health, Labour and Welfare, according to the GRADE method, and endorsed by the JCR. This unique set of recommendations and algorithms is expected to help patients with RA and health professionals choose treatment options in various clinical settings, especially when residual limb joint symptoms or functional impairment exist, even after sufficient and continuous drug treatment.

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# Supplementary data

Supplementary data is available at Modern Rheumatology online.

# **Conflict of interest**

The COI is disclosed only for voting CPG panellists as follows. H.I. belonged to the department that is financially supported by Nagahama city, Toyooka city, and five pharmaceutical Companies (Mitsubishi Tanabe Pharma Co., Chugai Pharmaceutical Co. Ltd, UCB Japan Co., Ayumi Pharmaceutical Corp., and Asahi Kasei Pharma Corp. H.I. has received research grants from AbbVie GK, Bristol Myers Squibb Co., Eisai Co., Ltd, Taisho Pharmaceutical Co., Ltd, and Mochida Pharmaceutical Co., Ltd. K.N. has received research grants and/or speaker's fee from AbbVie GK, Asahi Kasei Pharma Corp, Chugai Pharmaceutical Co. Ltd, Daiichi-Sankyo, Inc., Eisai Co., Ltd, Mitsubishi Tanabe Pharma Co., Eli Lilly Japan K.K., and Ono Pharmaceutical Co. T.K. has received research grants from AbbVie GK, Astellas Pharma Inc., Chugai Pharmaceutical Co. Ltd, Eli Lilly Japan K.K. T.K. has received speaker's fee from AbbVie GK, Asahi Kasei Pharma Corp., Ayumi Pharmaceutical Corp., Boehringer Ingelheim Japan, Inc., Bristol Myers Squibb Co., Chugai Pharmaceutical Co., Ltd, Daiichi-Sankyo, Inc., Eisai Co., Ltd, Eli Lilly Japan K.K., and Pfizer Japan Inc., and UCB Japan Co. I.M. has received speaker's fee from Bristol Myers Squibb Co., and Chugai Pharmaceutical Co. Ltd. M.K. has received Consulting fees and/or speaker fees from AbbVie GK, Amgen Inc., Asahi Kasei Pharma Corp, Astellas Pharma Inc., Ayumi Pharmaceutical Corp., Bristol Myers Squibb Co., Chugai Pharmaceutical Co. Ltd, Daiichi-Sankyo, Inc., Eisai Co., Ltd, Eli Lilly Japan K.K. Gilead Sciences, Inc., Janssen Pharmaceutical K.K., Novartis Pharma K.K, Ono Pharmaceutical Co., Pfizer Japan Inc., Tanabe-Mitsubishi Pharma Co., and UCB Japan Co. S.H. has received speaker's fee, Consultancy fee, research grant, or honoraria from AbbVie GK, Asahi Kasei Pharma Corp., Astellas Pharma Inc., Ayumi Pharmaceutical Corp., Bristol Myers Squibb Co., Celgene Corp., Chugai Pharmaceutical Co. Ltd, Eisai Co., Ltd, Gilead Sciences, Inc., GlaxoSmithKline K.K., Eli Lilly Japan K.K., Janssen Pharmaceutical K.K., Kyorin Pharmaceutical Co., Ltd, Novartis Pharma K.K., Pfizer Japan Inc., Sanofi Japan K.K., Mitsubishi Tanabe Pharma Co., UCB Japan Co. Y.K. (Yuko Kaneko) has received speaker's fee from AbbVie GK, Asahi Kasei Pharma Corp., Astellas Pharma Inc., Boehringer Ingelheim Japan, Inc., Bristol Myers Squibb Co., Chugai Pharmaceutical Co. Ltd, Eisai Co., Ltd, Novartis Pharma K.K., Pfizer Japan Inc., UCB Japan Co., and Janssen Pharmaceutical K.K. Y.K. (Yuko Kaneko) has received research grants from AbbVie GK, Eisai Co., Ltd, and Sanofi Japan K.K. M.M. belongs to the department that is financially supported by AbbVie GK, Asahi Kasei Pharma Corp, Ayumi Pharmaceutical Corp., Chugai Pharmaceutical Co. Ltd, CSL Behring LLC., Japan Blood Products Organization, Mitsubishi Tanabe Pharma Co., Nippon Kayaku Co. Ltd, Ono Pharmaceutical Co. Ltd, Towa Pharmaceutical Co. Ltd, and UCB Japan Co. Ltd, and has received lecture fee from AbbVie GK, Astellas Pharma Inc., Japan Vaccine. Novartis Pharma K.K., Swedish Orphan Biovitrum AB. and MSD K.K., and Consulting fee from Daiichi-Sankyo, Inc. and Taisho Pharmaceutical Co., Ltd. A.M. (Akio Morinobu) has received speaking fees from AbbVie GK, Chugai Pharmaceutical Co. Ltd, Eli Lilly Japan K.K., Eisai Co., Ltd, Ono Pharmaceutical Co., Pfizer Japan Inc., and Takeda Pharmaceutical Company Ltd. A.M. (Akio Morinobu) has received research grants from AbbVie GK, Asahi Kasei Pharma Corp., Eli Lilly Japan K.K., Astellas Pharma Inc., Chugai Pharmaceutical Co. Ltd, Ono Pharmaceutical Co., Takeda Pharmaceutical Co. Ltd, Mitsubishi Tanabe Pharma Co. and Bristol-Myers Squibb Co. Y.S. has received speaking fee from AbbVie G.K. A.M. (Atsuko Murashima) has received unrestricted research grants from Chugai Pharmaceutical Co. Ltd, and has received speaker bureaus from Chugai Pharmaceutical Co. Ltd, Bristol Myers Squibb Co., Astellas Pharma Inc., UCB Japan Co. Ltd, and Mitsubishi Tanabe Pharma Co. T.S. has received research grants from Asahi Kasei Pharma Corp., Daiichi-Sankyo, Inc., and Ono Pharmaceutical Co. T.S. has received

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