Appendix 1: Recommendations for the treatment of established rheumatoid arthritis.

[Source: Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken)* 2012;64:625-39. Copyright © 2012 American College of Rheumatology. Reprinted with permission from John Wiley & Sons, Inc.]

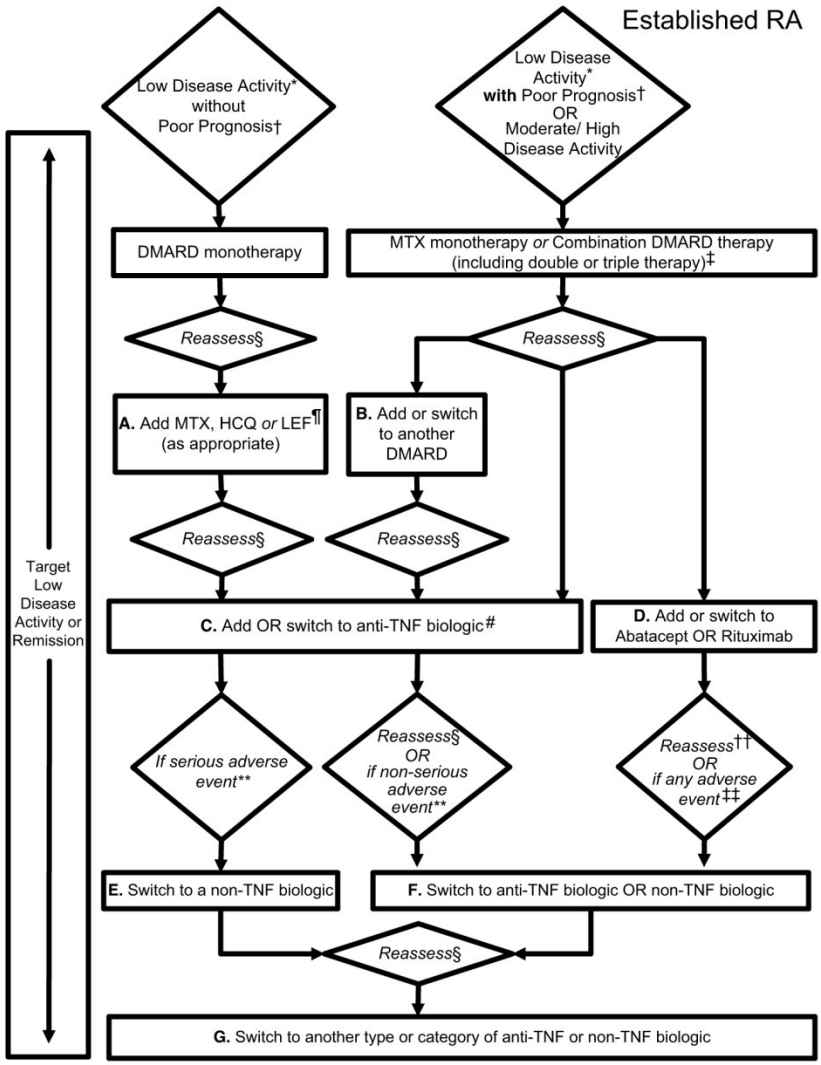

Figure 2. 2012 American College of Rheumatology (ACR) recommendations update for the treatment of established rheumatoid arthritis (RA), defined as a disease duration ≥6 months or meeting the 1987 ACR classification criteria. Depending on a patient's current medication regimen, the management algorithm may begin at an appropriate rectangle in the figure, rather than only at the top of the figure. Disease-modifying antirheumatic drugs (DMARDs) include hydroxychloroquine (HCQ), leflunomide (LEF), methotrexate (MTX), minocycline, and sulfasalazine (therapies are listed alphabetically; azathioprine and cyclosporine were considered but not included). DMARD monotherapy refers to treatment in most instances with HCQ, LEF, MTX, or sulfasalazine; in few instances, where appropriate, minocycline may also be used. Anti–tumor necrosis factor (anti-TNF) biologics include adalimumab, certolizumab pegol, etanercept, infliximab, and golimumab. Non-TNF biologics include abatacept, rituximab, or tocilizumab (therapies are listed alphabetically). For the level of evidence supporting each recommendation, please see Supplementary Appendix 7 (available in the online version of this article at http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)2151-4658).

* Definitions of disease activity are discussed in Tables 2 and 3 and Supplementary Appendix 4 (available in the online version of this article at http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)2151-4658) and were categorized as low, moderate, or high.

† Features of poor prognosis included the presence of 1 or more of the following: functional limitation (e.g., Health Assessment Questionnaire score or similar valid tools), extraarticular disease (e.g., presence of rheumatoid nodules, RA vasculitis, Felty's syndrome), positive rheumatoid factor or anti–cyclic citrullinated peptide antibodies (33–37), and bony erosions by radiograph (38).

‡ Combination DMARD therapy with 2 DMARDs, which is most commonly MTX based, with few exceptions (e.g., MTX + HCQ, MTX + LEF, MTX + sulfasalazine, sulfasalazine + HCQ), and triple therapy (MTX + HCQ + sulfasalazine).

§ Reassess after 3 months and proceed with escalating therapy if moderate or high disease activity in all instances except after treatment with a non-TNF biologic (rectangle D), where reassessment is recommended at 6 months due to a longer anticipated time for peak effect.

¶ LEF can be added in patients with low disease activity after 3–6 months of minocycline, HCQ, MTX, or sulfasalazine.

If after 3 months of intensified DMARD combination therapy or after a second DMARD has failed, the option is to add or switch to an anti-TNF biologic.

** Serious adverse events were defined per the US Food and Drug Administration (FDA; see below); all other adverse events were considered nonserious adverse events.

†† Reassessment after treatment with a non-TNF biologic is recommended at 6 months due to anticipation that a longer time to peak effect is needed for non-TNF compared to anti-TNF biologics.

‡‡ Any adverse event was defined as per the US FDA as any undesirable experience associated with the use of a medical product in a patient. The FDA definition of serious adverse event includes death, life-threatening event, initial or prolonged hospitalization, disability, congenital anomaly, or an adverse event requiring intervention to prevent permanent impairment or damage.

Appendix to: Singh JA. Use of biologics in a patient with rheumatoid arthritis refractory to methotrexate. *CMAJ* 2013. DOI:10.1503/cmaj.121607.