

Vaccination recommendations for adult patients with rheumatic diseases

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Abstract

Infectious diseases in any age group can be successfully prevented through immunization. Protection provided through immunization in childhood decreases over the years. Immunization in adulthood is important because of the growing elderly population, chronic diseases, and globalization. Recommendations on this subject are being constantly updated through scientific guidelines. Immunization in adulthood is also important in rheumatology. There is an increased risk not only of infection in rheumatic diseases but also of infections being more severe. Most infections, and their frequently observed complications, are among those diseases that can be prevented through immunization. The type of immunization, immunosuppressive/immunomodulatory therapy received by the patient, disease activity, and presence of chronic diseases affect the immunization process in patients with rheumatic diseases. This review will consider the immunization process followed in rheumatic diseases and also refer to its application.

Keywords: Vaccination, adult, rheumatic disease



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The basic principles of adult vaccination

Vaccines are among the greatest achievements of modern medicine. The most effective way to prevent infectious diseases in any age group is immunization. The protection provided by vaccines during childhood decreases with age. The concept of immune senescence is defined as “changes that reduce the protection of the vaccines as a result of aging and the effects of aging on natural and acquired immunities” (1). Moreover, the incidence and burden of vaccine-preventable diseases in adulthood are increasing because of the significantly increasing elderly population (2), burden of chronic diseases, globalization, and the introduction of less effective vaccines with fewer side effects. Although considered as merely childhood diseases for many years, currently, vaccine-preventable infections may cause serious morbidity and mortality in adults. For example, over the years, the numbers of tetanus cases have been decreasing because of pregnancy immunization programs for the prevention of maternal and neonatal tetanus. However, on closer inspection, it becomes apparent that fatal cases of tetanus are seen in adulthood, and the incidence of death reaches the highest rates in people over 80 years of age (3). When pertussis cases were analyzed in the United Kingdom, it was evident that the incidence of this disease has increased four-fold between 2008 and 2012, and the majority of the cases involved people over the age of 15 years (4). In 2014, the Centers for Disease Control and Prevention announced that the United States experienced the largest pertussis epidemic in the last 50 years (5). The measles outbreak in Europe starting at the end of 2009 in Bulgaria led to many deaths and thousands of cases of the disease (6). Turkey was also affected by this epidemic, such that young adults, who were vaccinated with only one dose of measles vaccine in their childhood between the years 1987 and 1998, were admitted to hospitals with severe measles manifestations (7).

Scientific guidelines for adult vaccination are constantly updated. The United States Advisory Committee on Immunization Practices updates its current vaccination guidelines annually (8). The National Adult Immunization Guideline was published in 2009 to create a vaccination framework for Turkey (9) and has been updated for the year 2015.

Adult vaccination in rheumatic diseases

Adults with rheumatic diseases have a special place among patients who are indicated for vaccination. Infectious diseases have increased the morbidity and mortality in patients with rheumatic diseases because of their natural history or the associated complications (such as splenic infarcts and skin ulcers), concomitant chronic diseases, immunosuppressive and immunomodulatory drug use, frequent hospitalization, and surgery. Rheumatic diseases increase not only the risk of infection but also the risk for a more severe course (10). A study involving 46,000 patients with rheumatoid arthritis and matched controls reported that the

complications of influenza were increased 2.75 folds in patients with rheumatoid arthritis than in those without the condition (11), and this risk has been reported to be independent of the drug used. The influenza vaccine has been shown to reduce the severity of the disease or attack rate regardless of the treatment given (12). On the other hand, the infection itself and the discontinuation of immunosuppressive therapy in the period of infection can lead to exacerbations of the autoimmune disease. The infections that are common and cause complications in rheumatic diseases are usually vaccine-preventable diseases. In particular, influenza, invasive pneumococcal diseases, tetanus–diphtheria, herpes zoster, and—considering the prevalence in Turkey—hepatitis A and B seem to be appropriate targets for vaccination (Table 1).

A number of factors affect the efficacy of vaccines administered to adult patients with rheumatic diseases:

- Type of vaccine
- Immunosuppressive/immunomodulatory therapy
- Disease activity

- Factors that apply to other healthy individuals, such as age and presence of chronic diseases

Generally applicable recommendations do not exist for the highly utilized biological agents of today, such as tumor necrosis factor (TNF) inhibitors, rituximab, abatacept, tocilizumab, ustekinumab, anakinra, and tocilizumab. One thing that is definite is that live vaccines are contraindicated during treatment with these agents.

Many cross-sectional and prospective cohorts investigating whether vaccines lead to the exacerbation of existing autoimmune diseases have demonstrated the safety of vaccines (13, 14). The risk of flare caused by infection is often greater than the risks caused by vaccination. For example, in the 2009/10 H1N1 pandemic, AS03-H1N1 vaccine was administered to 90 patients with juvenile idiopathic arthritis. In 59% of the patients receiving methotrexate and in 24% of those receiving etanercept, no change in disease activity was observed for 4 weeks after vaccination. The disease flare rate in that study was found to decrease from 4.8% to 4.4% (15). Similar results were obtained in a

group of patients with multiple sclerosis. The rate of vaccination within the previous two months was found to be 2.3% among patients with relapsing disease and 2.8%–4.0% in those with stable disease (16). In another study, it was found that the risk of relapse was much higher for infections than for vaccinations (17).

Inactive vaccines

Recombinant or inactivated vaccines do not pose a risk of infection, but they induce a suboptimal immune response and would often need an adjuvant, or a booster dose (Table 2). In order to avoid generating a conflict with regards to vaccine safety and to induce an adequate immune response, it is recommended to administer the inactivated vaccines during the lowest level of disease activity, before the immunosuppressive therapy is initiated, or under low-dose immunosuppressive therapy. Two weeks are required for the development of an immune response. Therefore, if possible, inactivated vaccines should be administered at least 2 weeks before the commencement of immunosuppressive therapy without delaying the treatment

Table 1. Vaccination scheme in adults with rheumatic diseases

Vaccine	18–64 years	≥65 years
Influenza	1 dose annually	
^{1,2} Pneumococcal (polysaccharide/conjugate)	1–2 doses	1–2 doses
³ Tetanus, diphtheria (Td)	A booster dose of vaccine every 10 years	
Hepatitis B	3 doses (0, 1, and 6 months) [May need to be applied as high-dose vaccine (0, 1, 2, and 6 Months) and double doses of vaccine in high risk patients who are going to receive biological agents or medium to high dose corticosteroids depending on the serological status]	
Hepatitis A	2 doses of vaccine (0 and 6 months)	
⁴ Varicella/Herpes zoster	Contraindicated in persons with immunosuppression: can be administered in consultation with a specialist in specific cases	
⁴ Measles, mumps, rubella (MMR)	Contraindicated in persons with immunosuppression: can be administered in consultation with a specialist in specific cases	
² Meningococcal (quadrivalent conjugate meningococcal vaccine)	2 doses of vaccine at least 2 months apart Can be repeated every 5 years if at continued risk	
² Haemophilus influenzae type B	1 dose	
⁵ Human papillomavirus (HPV)	2 or 3 doses	

Legend:
 Individuals who do not have immunity and contraindications
 Individuals who have risk factors and don't have contraindications

¹It is recommended to comply with the schedule for the polysaccharide and conjugate pneumococcal vaccines (recommendations with regards to risk groups are summarized in Table 2).

²In cases of asplenia (including elective splenectomy and persistent complement deficiencies).

³Scheme in persons who have completed the primary immunization for tetanus vaccine.

(Many guidelines recommend that one of the doses of Td every 10-years starting from the adolescence should be replaced with tetanus-diphtheria-acellular pertussis vaccine).

⁴Contraindicated in pregnancy.

⁵HPV vaccination initiated between 9–13 years in girls and preferably completed before the start of sexual activity is the most cost-effective way to prevent cervical cancer. The Center for Disease Control and Prevention has set an upper age limit of 26 years for HPV vaccination.

Table 2. Specific recommendations for the vaccines in rheumatic diseases

Vaccine	Recom.	Contraindication	Notes
Seasonal influenza	Usual	Severe allergic reaction after a previous influenza vaccine or a vaccine component including egg protein (e.g., anaphylaxis).	<ul style="list-style-type: none"> • All patients should be vaccinated every year. • Inactivated influenza vaccine should be used. • Seasonal influenza and the pandemic influenza vaccine can be administered simultaneously. • It has been shown that methotrexate, tumor necrosis factor (TNF) inhibitors, rituximab, and abatacept decrease vaccine response. • No change in vaccine response was observed with tocilizumab in rheumatoid arthritis patients.
Pneumococcal	Usual	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis).	<ul style="list-style-type: none"> • It is recommended in adults aged 65 years or older and in adults aged 19–64 years with risk factors (immunosuppression, asplenia, diabetes, chronic lung, and cardiovascular diseases, chronic liver disease, nephrotic syndrome, disseminated malignancy/hematological malignancies, cerebrospinal fluid leak, cochlear implant). • Polysaccharide (PPSV23) or conjugate (PCV13) pneumococcal vaccines can be used. The government pays for PPSV23 for patients with risk factors in Turkey; PCV13 can be administered with a doctor's written consent and request. The immune response to PCV13 is shown to be superior, therefore PCV13 has been prioritized in international guidelines (8, 20). • Only a single dose of PCV13 vaccine is recommended in adult life. PPSV23 can be repeated with regards to the algorithms specified below (24). <ul style="list-style-type: none"> - Adults aged 65 years or older who have not received the pneumococcal vaccine and who are not immunocompromised: Administer one dose of PCV13 or one dose of PPSV23. There should be at least 1 year between the two doses. It does not matter which one comes first. - Adults aged 19–64 years with chronic diseases excluding asplenia, immunosuppression, cerebrospinal fluid leak, and cochlear implant: Administer one dose of PPSV23 vaccine. - Adults who have received PPSV23 before the age of 65 years: administer one dose of PCV13 and one dose of PPSV23 at least 1 year after PCV13. There should be at least 5 years between the previous PPSV23 dose and the PPSV23 dose that is to be received after age 65 years. - Adults aged 19 years and older with functional or anatomical asplenia or with immunocompromising conditions: If vaccination has been started with PCV13, administer one dose of PPSV23 at least 8 weeks after PCV13. If vaccination has been started with PPSV23, administer PCV13 at least 1 year after PPSV23. If it has been 5 years since the first PPSV23 dose before the age of 65 years, administer a second dose of PPSV23. After the age of 65 years, administer a third dose of PPSV23 after 5 years has elapsed from the previous PPSV23 dose. However, PCV13 should not be repeated. • The pathogenetic mechanism blamed in Behcet's disease (BD) involves streptococcal sensitivity and a severe inflammatory syndrome has been reported to occur after the PPSV23 vaccine in patients with BD (25). Therefore, caution is warranted when planning pneumococcal vaccine in patients with BD. • Methotrexate, rituximab, and abatacept were shown to decrease vaccine response. The results with TNF inhibitors are contradictory. • Tocilizumab in rheumatoid arthritis and ustekinumab in psoriatic arthritis patients did not change the vaccine response to PPSV23.
Tetanus, Diphtheria (Td)/ Tetanus-Diphtheria-Acellular pertussis (Tdap)	Usual	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis). For pertussis-containing vaccines:	<ul style="list-style-type: none"> • Passive immunization with tetanus immunoglobulin is required in cases of suspected exposure if the patient has a history of rituximab infusion in the past 24 weeks.

Table 2. Specific recommendations for the vaccines in rheumatic diseases (Continued)

		encephalopathy not linked to other known causes, within 7 days after a Tdap [diphtheria, tetanus toxoid, and pertussis (DTP)] or DTaP (diphtheria and tetanus toxoids and acellular pertussis) vaccine (such as coma, seizures or prolonged decline in mental status).	
Hepatitis B	Usual	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis).	<ul style="list-style-type: none"> • Please refer to the Viral Hepatitis Screening Guideline Before Biological Drug Use in Rheumatic Patients (26).
Hepatitis A	Usual	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis).	<ul style="list-style-type: none"> • Risk of fulminant hepatitis is increased in cases with hepatitis-associated macrophage activation syndrome and chronic nonsteroidal anti-inflammatory drug use. • A single dose of hepatitis A vaccine is routinely recommended for immunization before travel to endemic areas. However the response to vaccine maybe insufficient in patients taking TNF inhibitors and/or methotrexate. Therefore, two doses of vaccine 6 months apart should be administered to these specific cases.
Meningococcal	Usual	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis).	<ul style="list-style-type: none"> • Methotrexate, azothioprine (no change or decreased response), TNF inhibitors (no change or decreased response), abatacept, rituximab, and tofacitinib may decrease vaccine response. Vaccination should be commenced before these drugs are initiated.
Human papillomavirus (HPV)	Usual	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis).	<ul style="list-style-type: none"> • HPV-associated cervical cancer risk is significantly increased in patients with systemic lupus erythematosus. • Some research indicates an increased venous thromboembolism risk with the quadrivalent vaccine.
Varicella/ Herpes zoster	Live vaccine recom.	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis). Known severe immune deficiency (hematologic and solid tumors, chemotherapy, long-term immunosuppressive therapy, or patients with severe immunosuppression of HIV infection). Pregnancy.	<ul style="list-style-type: none"> • Many scientific societies and committees agree that Herpes zoster vaccine is completely contraindicated in patients receiving immunosuppressive/modulatory therapy. • However, in recent years, considering the significant risk of shingles in patients with immunosuppression, it is argued that Herpes zoster vaccine could be administered in some selected patients receiving low-dose immunosuppressive therapy (8, 13, 20). However, it should be noted that this is an expert opinion, is not based on strong scientific evidence, and all patients should be evaluated on their own risks. • Herpes zoster vaccine can be considered in patients taking low-dose immunosuppression (see text) after consulting an expert. • Vaccination is contraindicated in patients using biological agents, cyclosporin A, cyclophosphamide, high-dose systemic steroids (≥ 20 mg/day prednisone or equivalent, for longer than 2 weeks), high-dose methotrexate, azothioprine, mercaptopurine, leflunomide, or mycophenolate mofetil. • All of the components are contraindicated in patients receiving immunosuppressive/modulatory therapy. • For those patients at high risk, MMR vaccine can be considered in patients after consulting an expert.
Measles, rubella, mumps (MMR)	Live vaccine recom.	Severe allergic reaction after a previous vaccine or a vaccine component (e.g., anaphylaxis). Known severe immune deficiency (hematologic and solid tumors, chemotherapy, long-term immunosuppressive therapy, or patients with severe immunosuppression of HIV infection). Pregnancy.	<ul style="list-style-type: none"> • All of the components are contraindicated in patients receiving immunosuppressive/modulatory therapy. • For those patients at high risk, MMR vaccine can be considered in patients after consulting an expert.

Recommendation:

- Adult immunization scheme recommendations are valid for usual recommendations. See Table 1.
- There is no indication for Bacillus Calmette–Guérin (BCG) vaccine in adults as most of the tuberculosis cases in adulthood are due to the activation of latent tetanus cases. BCG vaccine cannot be administered to persons older than 6 years of age even if has not been administered before. The Tuberculosis Screening and Prophylaxis Algorithm of the Rheumatology Society of Turkey can be referred to for further information.
- Travel vaccination: Rheumatic patients should receive the vaccines as recommended for other people in the population in accordance with the recommendations for that particular area, however live vaccines should be avoided (Türkiye Hudut ve Sahiller Sağlık Genel Müdürlüğü <http://www.seyahatsagligi.gov.tr/Site/Asilar>). Before Haj and Umrah, a single dose of meningococcal vaccine should be administered 7–10 days prior to the trip. In Turkey, quadrivalent conjugated meningococcal vaccine is preferred for adults younger than 56 years of age, whereas polysaccharide vaccine is administered to those who are aged 56 or older. Severely immunosuppressed patients should avoid traveling to areas where yellow fever (for which there are live, attenuated vaccines) is endemic. If travel is unavoidable, the patient should be vaccinated some time after the cessation of the immunosuppressive therapy (in accordance with live vaccine recommendations and the drug used). For those who will travel to countries with high prevalence of diseases (such as South America, Africa, and India), typhoid vaccine should be administered as a parenteral Vi capsular polysaccharide vaccine instead of live oral vaccine as a single dose at least 1 week before the trip.

or otherwise at the discretion of the clinician. On the other hand, inactivated vaccines can be administered directly after the discontinuation of immunosuppressive/immunomodulatory drug. Exceptions to this rule are abatacept and rituximab therapies. The immune response was found to be low even 2 weeks after discontinuation of abatacept (18). It is recommended to wait for vaccination at least 6 months after rituximab infusion (19). However, if a vaccine, such as influenza, needs to be administered within a certain time interval, vaccination should be done, although lower vaccine effectiveness is expected.

The interaction of intravenous immunoglobulins (Ig) with inactivated vaccines and toxoids is unremarkable. Inactivated vaccines and Ig products may be administered simultaneously or within any time interval. An exception to this is the hepatitis A vaccine because the immune response to this vaccine was shown to be reduced when administered simultaneously with Ig. It is recommended to administer hepatitis A vaccine no earlier than 3 months after the administration of Ig.

Live vaccines

The use of live vaccines is generally contraindicated in patients being treated with an immunosuppressive/immunomodulatory drug because of the risk of infection that the vaccine strains can generate (20-22). However, if live vaccines are indicated for patients at risk, they may be used only after consulting a specialist (Table 1, 2). Live vaccines can be administered during sulfasalazine and hydroxychloroquine therapies.

The doses of corticosteroids which would pose a contraindication for live vaccines have been described as follows;

- ≥ 20 mg/day prednisone or equivalent, for longer than 2 weeks (≥ 10 mg/day prednisone or equivalent doses for longer than 2 weeks are considered as contraindication in some countries, including the United Kingdom.)

The risk of shingles is increased in rheumatic diseases. Therefore, some experts encourage the administration of Herpes zoster vaccine to patients under low-dose immunosuppressive therapy. However, it should be noted that the cumulative effects of more than one low-dose immunosuppressive drug could pose a contraindication for live vaccines. Low-dose immunosuppressive therapy can be defined as follows:

- Low-dose corticosteroid (< 20 mg/day of prednisone or equivalent, short or long term or alternating days),
- Glucocorticoid replacement therapy in adrenal insufficiency,
- Topical steroids or intra-articular, intra-bur-

sa, or intra-tendon steroid injection,

- Low-dose methotrexate (< 0.4 mg/kg/week or < 20 mg/week),
- Low dose azathioprine (< 3 mg/kg/day),
- Low dose 6-mercaptopurine (< 1.5 mg/kg/day)

The safe time intervals for the administration of live vaccines after cessation of immunosuppressive/immunomodulatory drugs generally vary depending on the pharmacodynamics features of the drugs. Live vaccines should be delayed for at least:

- 5 half-lives after the administration of biological agents or disease-modifying drugs (3–12 months),
- 4 weeks after high-dose corticosteroid therapy (≥ 20 mg/day prednisone or equivalent, for longer than 2 weeks),
- 4 weeks after etanercept and 3 months after other TNF inhibitors (infliximab, adalimumab),
- 4–12 weeks after the doses of ≥ 0.4 mg/kg/week or ≥ 20 mg/week of methotrexate (expert opinion is that there is no need to wait for Herpes zoster or Varicella zoster vaccine if the patient is on doses of methotrexate lower than 0.4 mg/kg/week or 20 mg/week),
- 6 to 12 months after rituximab (if possible, live vaccines should be canceled until the B cell count returns to normal levels),
- 2 years after leflunomide.

It is recommended that at least 4 weeks should elapse before the commencement of immunosuppressive therapy after the administration of the live vaccination. The immune response to live vaccines may be diminished when the vaccine is administered immediately before or after the infusion of Ig products. The interaction interval depends on the dose of Ig. Measles-mumps-rubella and varicella zoster vaccines should be administered either two weeks before the Ig therapy or should be delayed for 3–11 months after the therapy, depending on the dose of Ig. If a need for Ig therapy arises within 14 days after the vaccination, the vaccine should be re-administered 3–11 months after the Ig therapy in patients without serological evidence of an antibody response (23).

Recommendations:

Vaccination recommendations in adults with rheumatic diseases can be summarized as follows (8, 9, 13, 20-22).

- I. Each doctor visit should be an opportunity to inquire about vaccination history and to review the vaccination log of the patient.
- II. The vaccination status of a patient with rheumatic disease should be reviewed

immediately after the diagnosis. Any missing vaccines should be administered. The demographic characteristics of the patient, the profession, accompanying clinical conditions, and therapies (s)he receives should be questioned to assess the risks of infection and the indication for vaccination. Serological tests should be performed to assess the immune status of the patient if there are no vaccination records or if the vaccination history is unclear.

- III. National adult immunization recommendations also apply to patients with rheumatic diseases. The inactivated vaccines that need to be questioned at the first step are influenza, pneumococcal, tetanus-diphtheria, hepatitis B, and hepatitis A vaccines.
- IV. Pneumococcal, meningococcal, and *Haemophilus influenzae* type b vaccines should be questioned in patients with a risk of asplenia/hyposplenia and should be administered at least two weeks before an elective splenectomy operation.
- V. Vaccination should be completed before starting any immunosuppressive or immunomodulatory therapy. If the therapy has already been initiated, vaccines should be administered in the period of the lowest level of disease activity and the lowest dose of immunosuppressive therapy. Sulfasalazine and hydroxychloroquine do not affect the immune response and are not regarded as immunosuppressive therapy.
- VI. Vaccines administered according to guidelines are effective in preventing the risk of infection and are safe for use in rheumatic diseases. There is no evidence that vaccines induce a rheumatic disease or cause an exacerbation of an existing rheumatologic disease.
- VII. There is no contraindication for the administration of inactive or live vaccines in rheumatic patients who are not under immunosuppressive therapy.
- VIII. Inactivated vaccines can be used in patients receiving immunosuppressive therapy. Although there is no concern about safety, it is generally recommended to administer the inactive vaccines during the lowest level of disease activity and the lowest dose of immunosuppressive therapy to have a better response to vaccination. Inactivated vaccines, if possible, should be given at least 2 weeks before the therapy is started.
- IX. Corticosteroids and non-biological disease-modifying agents other than methotrexate do not markedly reduce the immune response to the inactivated vac-

- cines. Methotrexate and in some studies TNF inhibitors were shown to reduce the immune response to pneumococcal vaccines and to influenza vaccine.
- X. Rituximab significantly reduces the immune response to inactive vaccines. Clinicians should delay the vaccination at least for 6 months after the last infusion. Abatacept also significantly reduces the immune response to inactive vaccines.
- XI. Live vaccines should be avoided as much as possible in patients under immunosuppressive therapy. However, every patient should be individually evaluated with regards to certain risks (such as the age, state of epidemic, drug type, and drug dosage).
- XII. Live vaccines should be administered in consultation with an expert. Generally speaking, immunosuppressive therapy should be started at least 4 weeks after the administration of live vaccines. On the other hand, the time to administer a live vaccine after discontinuation of immunosuppressive therapy should be determined considering factors such as the currently used immunosuppressive/modulatory drug dose and its half-life or mechanism of action. Additionally, the availability of antimicrobial and/or Ig therapies in case of the possibility of a vaccine-related infection should be assessed while deciding to administer a live vaccine.
- XIII. Herpes zoster, Varicella zoster, and measles-mumps-rubella vaccines are contraindicated in patients receiving immunosuppressive therapy. However, the risk of shingles and post-herpetic neuralgia is significantly high in immunocompromised patients. Further studies are needed to evaluate the safety and effectiveness of the Herpes zoster vaccine in certain rheumatic patients under immunosuppressive therapy.
- XIV. The efficacy of booster vaccination during immunosuppressive therapy does not change significantly in those patients who completed their childhood or primary vaccination series.
- XV. Serologic response to immunization can be controlled 4–6 weeks after the vaccination if there is a valid serological method.
- XVI. If a patient cannot be vaccinated because of certain reasons, people who are in close contact with the patient can be vaccinated to reduce the risk of infection. However, such cases should be referred to a specialist before using live vaccines.
- XVII. Institutions can adopt a strategy, applied through the collaboration of doctors, nurses, and secretaries, for inquiring about

- vaccine history and launching vaccination logs. Reminders and decision support systems can be integrated to electronic healthcare records.
- XVIII. Patients with rheumatic disease can be informed about the importance and the safety of vaccines and about the current vaccination recommendations using verbal communication or written leaflets to improve health literacy.
- XIX. Scientific knowledge on the efficacy, effectiveness, and safety of vaccination is gradually increasing along with the accumulating data on the vaccines and the treatment options in rheumatic diseases. Therefore, the expert councils should periodically revise the literature and update their vaccination recommendations for adults with rheumatic diseases.

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