SUPPLEMENTARY APPENDIX 2: PICO Questions

2022 American College of Rheumatology (ACR) Guideline for Vaccinations in Patients with Rheumatic and Musculoskeletal Diseases

RISKS OF VACCINE-PREVENTABLE DISEASE (INCLUDING CERVICAL/ANAL CANCER FROM HPV)

Prognosis rather than intervention questions

1. Are patients with RMD disease X at increased risk *to contract* vaccine-preventable diseases compared to the general population?

P - RMD patients
C - General population
O - Contracting vaccine-preventable diseases

2. Are patients with RMD disease X at increased risk *for more severe outcomes from* vaccine-preventable diseases compared to the general population?

P - RMD patients
C - General population
O - Outcomes (mortality/morbidity) from vaccine-preventable diseases (will include all markers of severity, e.g., hospitalization, death)

QUESTIONS REGARDING VACCINE IMMUNOGENICITY/EFFICACY/SAFETY TO INFORM GUIDELINE RECOMMENDATIONS

Prognosis rather than intervention questions

3. In patients with [RMD Disease X], what is the effect of [Drug Y/Drug Class] on immunization responses to [Vaccine Z, Vaccine Type] in comparison with [General population, or Drug Y']?

P - RMD Disease X
I - Vaccine Z
C 1 - Patients receiving drug(s) Y
C 2 - Patients receiving drug(s) Y
C 3 - Healthy controls

O - Immunogenicity (Geometric mean titer (GMT), fold increase in titer, seroconversion, seroprotection, cell mediated immunity)

4. In RMD patients, does the immunogenicity or efficacy of Vaccine Z differ in patients taking high-dose steroids as compared to those using lower doses of steroids or those not using steroids?

P - RMD patients taking high dose steroids I - Vaccine Z
C 1- RMD patients taking low dose steroids
C 2 - RMD patients not taking steroids

O - Rates of infection, immunogenicity

5. In RMD patients on drug Y, do immune responses to neo-antigens (not vaccines) differ from responses seen in the general population?
P - RMD patients receiving drug Y
I - Administration of neo-antigen
C 1 - Administration of neo-antigen to general population
C 2 - Administration of neo-antigen to RMD patients not receiving Drug Y
O – Immunogenicity

6. In patients with [Disease X], is the duration of the immune response to [Vaccine Z] diminished compared to [healthy controls]?
P - Disease X
I - Vaccine Z
C 1 - Patients receiving drug(s)
C 2 - Healthy controls
O - Immunogenicity (see question #2), development of vaccine-preventable disease

[NOTE: PICO 7 was in the original project plan, but it was removed mid-way through the project, so it was not included in the final evidence report.]

7. Do patients with [Disease X] have higher rates of adverse events following [Vaccine Z] compared to [healthy controls]?
P - Disease X
I - Vaccine Z
C 1 - Patients receiving drug(s) Y
C 2 - Healthy controls

O - Reactogenicity (fever, vaccine site reactions, myalgia, arthralgia, headache, rhinitis, sore throat)

8. Do patients with [Disease X] experience flares of their underlying RMD after immunization with [Vaccine Z]?
P - RMD Disease X
I - Administer Vaccine Z
C - Do not administer vaccine Z
O - Increase in disease activity

QUESTIONS ABOUT ANNUAL INFLUENZA VACCINE

9. In RMD patients age 65 and older, is high dose (Fluzone high dose) influenza vaccine more effective than seasonal regular dose influenza vaccine?

P - Patients with RMD age 65 and older
I - High dose (Fluzone) influenza vaccine
C - Regular dose influenza vaccine
O - Rates of influenza infection, immunogenicity reactogenicity

10. In RMD patients age 65 and older, is adjuvanted influenza vaccine (FLUAD) more effective than seasonal regular dose influenza vaccine?

P - Patients with RMD age 65 and older
I - FLUAD influenza vaccine
C - Regular dose influenza vaccine
O - Rates of influenza infection, immunogenicity, reactogenicity

11. In RMD patients *under* age 65 years, is high dose (Fluzone high dose) vaccine more effective than seasonal regular dose influenza vaccine?

P - Patients with RMD underage 65
I - Fluzone high dose influenza vaccine
C - Regular dose influenza vaccine
O - Rates of influenza infection, immunogenicity, reactogenicity

12. In RMD patients *under* age 65 years, is adjuvanted influenza vaccine (FLUAD) more effective than seasonal regular dose influenza vaccine?

P - Patients with RMD under age 65
I - FLUAD adjuvanted influenza vaccine
C - Regular dose influenza vaccine
O - Rates of influenza infection, immunogenicity, reactogenicity

13. In RMD patients, does the immunogenicity or efficacy of influenza vaccine differ in patients who have moderate to severely active underlying disease as compared to those in low-disease activity or remission?

P - Patients with moderate to severely active RMD
I - Influenza vaccination
C - Patients with quiescent/low disease activity RMD
O - Rates of influenza infection, immunogenicity

14. In RMD patients, does the immunogenicity or efficacy of influenza vaccine differ in patients taking high dose steroids as compared to those using lower doses of steroids or those not using steroids?

P - RMD patients taking high dose steroids
I - Influenza vaccination
C 1 - RMD patients taking low dose steroids
C 2 - RMD patients not taking steroids
O - Rates of influenza infection, immunogenicity

15. In RMD patients, does the immunogenicity or efficacy of influenza vaccine differ in patients taking Drug Y as compared to those not using drug Y at the time of vaccination?
P - RMD patients taking Drug Y
I - Influenza vaccination
C - RMD patients not taking drug Y
O - Rates of influenza infection, immunogenicity

QUESTIONS ABOUT TIMING OF VACCINE WITH RESPECT TO IMMUNOSUPPRESSIVE MEDICATIONS OR DISEASE ACTIVITY

16. Should patients with RMD taking drug Y hold their drug for a period of time prior to or after receiving (not live-attenuated) vaccines?
P - Patients with RMD on drug Y
I 1 - Hold drug Y prior to vaccine
I 2 - Hold drug Y after vaccine
C - Usual dosing of drug Y
O - Reactogenicity, disease flare, immunogenicity

17. Should patients with RMD who are taking biologic medications with usual dosing schedules of monthly or longer* schedule (not live-attenuated) vaccine administration relative to next dose of medication?
P - Patients with RMD on intermittent-dosing biologic medications
I 1 - Vaccination 1 month before next biologic medication dose
I 2 - Vaccination > 1 month before next biologic medication dose
C - No schedule adjustment of vaccine relative to medication dose
O - Reactogenicity, disease flare, immunogenicity

*Rituximab, ocrelizumab, belimumab, ustekinumab, tocilizumab (IV), TNF inhibitors (infliximab, golimumab, certolizumab), IVIg, abatacept (IV), secukinumab, ixekizumab, guselkumab, canakinumab, tildrakizumab, risankizumab

18. Should moderately to severely ill RMD patients with disease X defer vaccination (for NOT live-attenuated) until disease is better controlled?
P - RMD patients with moderate to severe active disease
I - Delay vaccine until low disease activity or remission

C - Proceed with vaccinations without change in schedule
O - Reactogenicity, immunogenicity

QUESTIONS RELATED TO VACCINATION OUTSIDE OF STANDARDIZED AGE RANGES

19. Should RMD patients be vaccinated against HPV at ages older than age 26?
P - RMD patients older than 26 without complete HPV vaccination
I - Vaccinate for HPV
C - Do not vaccinate for HPV
O - Rates of HPV infection, incidence of HPV-related cancer (cervical, anal, head and neck cancer)

20. Should RMD patients with RMD receive vaccination against pneumococcus at ages less than 65 years?
P - RMD patients under age 65 with RMD who have not received pneumococcal vaccine
I - Vaccinate against pneumococcus
C - No pneumococcal vaccination
O - Rates of pneumonia and associated complications, reactogenicity, immunogenicity

21. Should RMD patients receive Shingrix vaccine (against varicella zoster virus [VZV]) at ages younger than 50 years?

P - RMD patients under 50 years who have not received Shingrix
I - Administer Shingrix vaccine
C - Do not administer Shingrix vaccine
O - Rates of herpes zoster (shingles) and shingles-related complications (post herpetic neuralgia, disseminated herpes zoster infection), reactogenicity, immunogenicity

22. Should RMD patients receive standardized regimens of vaccine combinations?
P - RMD patients
I - Administer vaccines individually rather than in standardized combinations
C - Administer combination vaccines according to ACIP guidelines
O - Change in RMD disease activity

QUESTIONS REGARDING USE OF LIVE-ATTENUATED VACCINES

23. Should RMD patients taking drug Y receive live-attenuated vaccines?
P - RMD Patients taking drug Y
I - Receive live-attenuated vaccine
C - Do not receive live-attenuated vaccine
O - Development of vaccine-preventable infection

24. Should RMD patients taking drug Y hold the drug for a period of time prior to or after receiving live-attenuated vaccines?

P - RMD patients taking drug Y
I 1 - Hold drug Y prior to vaccination
I 2 - Hold drug Y after vaccination
C - No alterations in drug dosing
O - Development of vaccine-preventable infection

25. Should neonates/infants with second and third trimester antenatal exposure to TNF inhibitors or Rituximab receive live-attenuated rotavirus vaccine in their first 6 months of life?

P - neonates/infants with 2nd or 3rd trimester exposure to TNF inhibitors or Rituximab
I - Administer rotavirus vaccine in first 6 months of life
C 1 - Do not administer rotavirus vaccine
C 2 - Delay live-attenuated rotavirus vaccine until after first 6 months of life
O - Rates of rotavirus infection

26. Should family members of RMD patients receive live-attenuated vaccines?

P - Family member of RMD patients
I - Administration of live-attenuated vaccines
C - Do not administer live-attenuated vaccines
O - Development of vaccine-preventable infection