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RHEUMATOLOGY ADVANCED
PRACTICE PROVIDERS

Inaugural National Conference

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VIRTUAL CONFERENCE



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Vaccinating Patients on Biologic and Non-Biologic DMARDs: The What, When, and How

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Disclosure

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Vaccines & Rheumatology Objectives

- Describe the relevant components of the immune system in terms of how vaccines work.
- Understand why vaccination is vital to the care plan of rheumatic disease (RD) patients.
- Determine appropriate timing for vaccinations for patients on immunosuppressive therapy.
- Know which vaccinations are contraindicated in RD patients on immunosuppressive therapy.

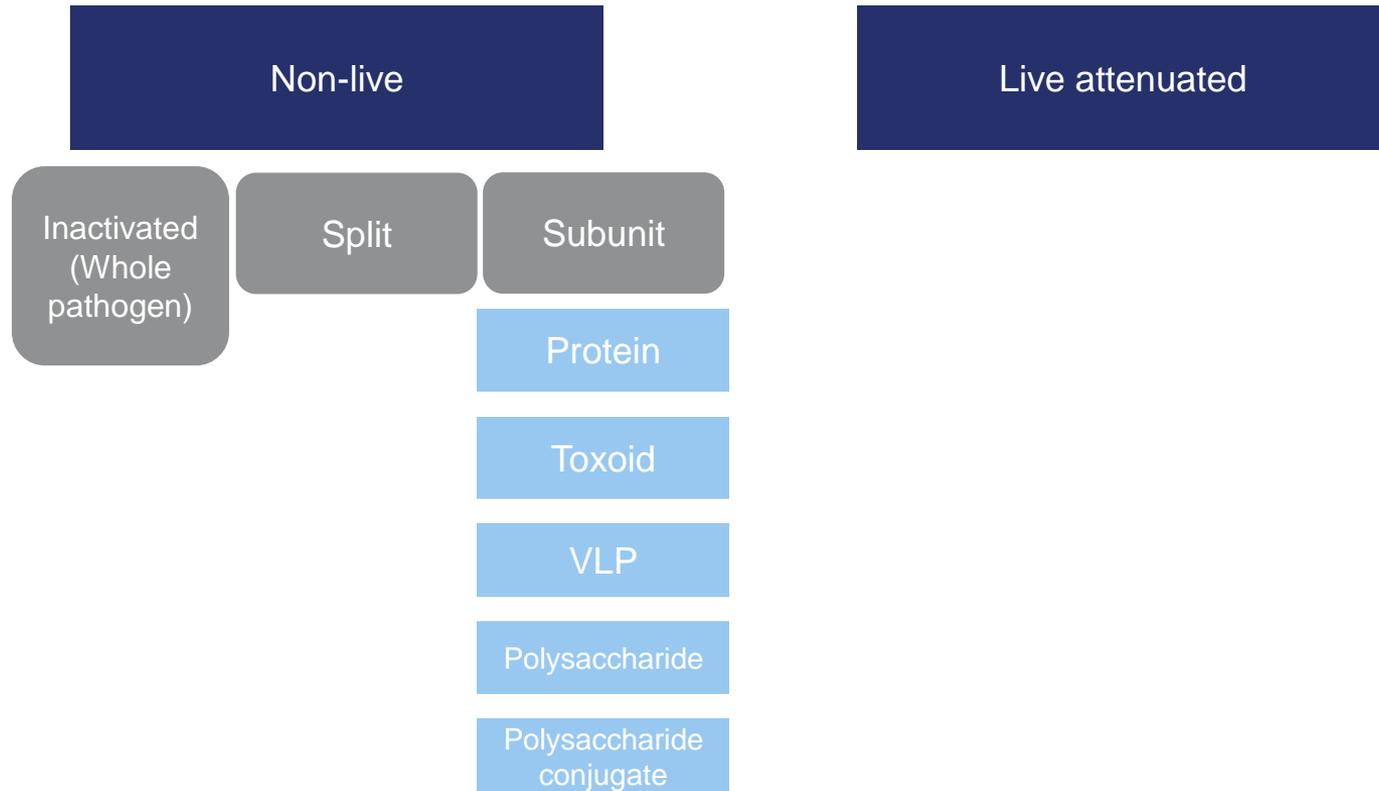
How Vaccines Work

- Step One: Initiate innate immune response
 - Fast, non-specific, “trained memory”
 - Macrophages
 - Complement proteins
 - Natural Killer Cells
- Step Two: Activate antigen-specific adaptive immune response
 - Later, specific, +memory
 - B Cells and Antibodies
 - T Cells and Cytokines

How Vaccines Work

- First encounter with invader → response takes several days
- After the first encounter, the immune system remembers what it learned about how to protect the body against that disease
 - T-lymphocytes (only a few) are kept around so they can go into action quickly if the body encounters the same germ again
 - When the familiar antigens are detected, B-lymphocytes produce antibodies to attack them
- **THIS IS THE POINT OF VACCINATION**

Types of Vaccines



Rheumatology Patients Differ From General Populations:

- Increased risk of infection
 - Disease related immune dysfunction
 - Immunosuppressive medication use
- More severe course of infection
- More hospitalizations
- Infections are a major cause of death
 - Patients with RA are 2x more likely to die from infections

Safety & Efficacy of Vaccination in Patients With Rheumatic Disease (RD)

- No specific contraindications for vaccination with inactivated and live vaccines in patients with RD but without immunosuppressive treatment.
- AVOID Live Vaccines in patients on immunosuppressants.

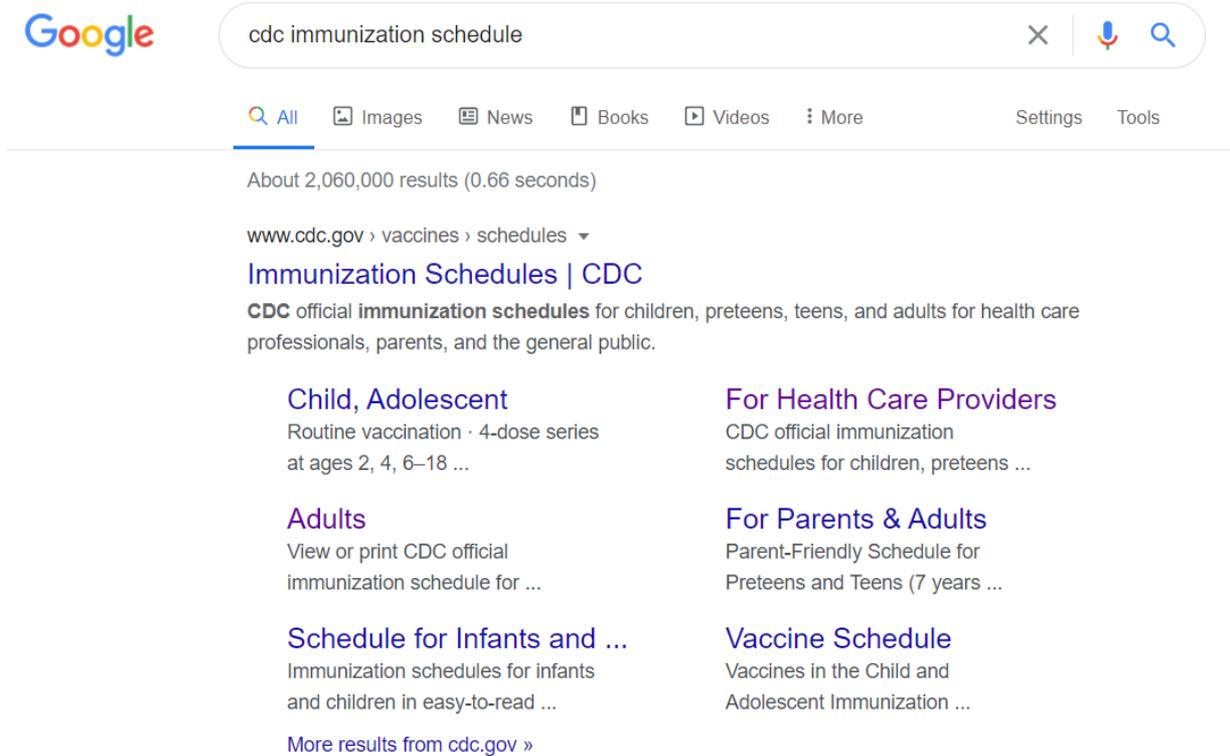
Safety & Efficacy of Vaccination in Patients With Rheumatic Disease (RD)

- Some protection is better than none!
- Vaccines are efficacious in patients with RD even when treated with DMARD, TNFs, TCZ, and ABA, but ideally should be given before B cell depleting biologics (e.g. rituximab).

When to Vaccinate

- Assess immunization status in the initial workup of every patient with RD.
- Ideally vaccination should be done only during stable disease.
- In severe RD cases, starting treatment is the main priority rather than early administration of vaccines.

Where to Find Immunization Schedules



Google

cdc immunization schedule

All Images News Books Videos More Settings Tools

About 2,060,000 results (0.66 seconds)

www.cdc.gov > [vaccines](#) > [schedules](#) ▾

Immunization Schedules | CDC

CDC official immunization schedules for children, preteens, teens, and adults for health care professionals, parents, and the general public.

<h3>Child, Adolescent</h3> <p>Routine vaccination · 4-dose series at ages 2, 4, 6–18 ...</p>	<h3>For Health Care Providers</h3> <p>CDC official immunization schedules for children, preteens ...</p>
<h3>Adults</h3> <p>View or print CDC official immunization schedule for ...</p>	<h3>For Parents & Adults</h3> <p>Parent-Friendly Schedule for Preteens and Teens (7 years ...</p>
<h3>Schedule for Infants and ...</h3> <p>Immunization schedules for infants and children in easy-to-read ...</p>	<h3>Vaccine Schedule</h3> <p>Vaccines in the Child and Adolescent Immunization ...</p>

[More results from cdc.gov »](#)

Adult Schedule

Immunization Schedules

CDC > Schedules Home > For Health Care Providers

Table 1. Recommended Adult Immunization Schedule for ages 19 years or older, United States, 2020

Always make recommendations by determining needed vaccines based on age (Table 1), assessing for medical conditions and other indications (Table 2), and reviewing special situations (Notes).

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Table 1. By age

Table 2. By indications

Schedule Changes & Guidance

Resources for health care providers

Resources for adults

Download schedules app

- 8.5"x11" print color [6 pages]
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- Compliant version of this schedule

- Vaccines in the Adult Immunization Schedule
- Learn how to display current schedules from your website.
- Hard copies of the schedule are available for free using the CDC-info on Demand order form.

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Table 2 Recommended Adult Immunization Schedule by Medical Condition and Other Indications, United States, 2020

Vaccine	Pregnancy	Immuno-compromised (excluding HIV infection)	HIV infection CD4 count		Asplenia, complement deficiencies	End-stage renal disease; or on hemodialysis	Heart or lung disease, alcoholism ¹	Chronic liver disease	Diabetes	Health care personnel ²	Men who have sex with men			
			<200	≥200										
IIV or RIV or LAIV			1 dose annually											
Tdap or Td	1 dose Tdap each pregnancy		1 dose Tdap, then Td or Tdap booster every 10 years											
MMR		NOT RECOMMENDED	1 or 2 doses depending on indication											
VAR		NOT RECOMMENDED	2 doses											
RZV (preferred) or ZVL	DELAY			2 doses at age ≥50 years or 1 dose at age ≥60 years										
HPV	DELAY	3 doses through age 26 years	2 or 3 doses through age 26 years											
PCV13			1 dose											
PPSV23			1, 2, or 3 doses depending on age and indication											
HepA				2 or 3 doses depending on vaccine										
HepB				2 or 3 doses depending on vaccine										
MenACWY			1 or 2 doses depending on indication, see notes for booster recommendations											
MenB	PRECAUTION		2 or 3 doses depending on vaccine and indication, see notes for booster recommendations											
Hib		3 doses HSCT ³ recipients only		1 dose										

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection
 Recommended vaccination for adults with an additional risk factor or another indication
 Precaution—vaccination might be indicated if benefit of protection outweighs risk of adverse reaction
 Delay vaccination until after pregnancy if vaccine is indicated
 Not recommended/contraindicated—vaccine should not be administered
 No recommendation/Not applicable

1. Precaution for LAIV does not apply to alcoholism; 2. See notes for influenza; hepatitis B; measles, mumps, and rubella; and varicella vaccinations; 3. Hematopoietic stem cell transplant.

Pediatric Schedule

CDC > Schedules Home > For Health Care Providers



Table 3. Recommended Child and Adolescent Immunization Schedule by Medical Indication, United States, 2020

Always make recommendations by determining needed vaccines based on age ([Table 1](#)), determining appropriate intervals for catch-up, if needed ([Table 2](#)), assessing for medical indications ([Table 3](#)), and reviewing special situations ([Notes](#)).

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Table 1. By age

Table 2. Catch-up
schedule

Table 3. By medical
indications

Schedule Changes &
Guidance

Parent-friendly
schedule

Resources for health
care providers

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- [Vaccinate the Child and Adolescent Immunization Schedule](#)
- [Learn how to display current schedules from your website.](#)

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Table 3

Recommended Child and Adolescent Immunization Schedule by Medical Indication, United States, 2020

Always use this table in conjunction with Table 1 and the notes that follow.

VACCINE	INDICATION									
	Pregnancy	Immunocompromised status (excluding HIV infection)	HIV infection CD4+ count ¹		Kidney failure, end-stage renal disease, or on hemodialysis	Heart disease or chronic lung disease	CSF leaks or cochlear implants	Asplenia or persistent complement component deficiencies	Chronic liver disease	Diabetes
			<15% and total CD4 cell count of <200/mm ³	≥15% and total CD4 cell count of ≥200/mm ³						
Hepatitis B	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Rotavirus	Yellow	Red	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Diphtheria, tetanus, & acellular pertussis (DTaP)	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
<i>Haemophilus influenzae</i> type b	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Pneumococcal conjugate	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Inactivated poliovirus	Orange	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Influenza (IV)	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
or Influenza (LAV)	Yellow	Red	Red	Red	Orange	Red	Red	Orange	Orange	Orange
Measles, mumps, rubella	Yellow	Red	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Varicella	Yellow	Red	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Hepatitis A	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Tetanus, diphtheria, & acellular pertussis (Tdap)	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Human papillomavirus	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Meningococcal ACWY	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Meningococcal B	Orange	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
Pneumococcal polysaccharide	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow

Vaccination according to the routine schedule recommended
 Recommended for persons with an additional risk factor for which the vaccine would be indicated
 Vaccination is recommended, and additional doses may be necessary based on medical condition. See Notes.
 Not recommended/contraindicated—vaccine should not be administered
 Precaution—vaccine might be indicated if benefit of protection outweighs risk of adverse reaction
 Delay vaccination until after pregnancy if vaccine indicated
 No recommendation/not applicable

- For additional information regarding HIV laboratory parameters and use of live vaccines, see the General Best Practice Guidelines for Immunization, “Altered Immunocompetence,” at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html and Table 4-1 (footnote D) at www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html;
- Severe Combined Immunodeficiency;
- LAV contraindicated for children 2-4 years of age with asthma or wheezing during the preceding 12 months.

Recommended Vaccinations for Adults With RD

- Planning to start immunosuppression or presently immunosuppressed require the following inactivated vaccines:
 - PCV 13 followed > 8 weeks later by the 23-valent PPSV23
 - Seasonal influenza vaccine (annually)

Timing of Vaccination With Live Vaccines

- Ideally administer ≥ 4 weeks prior to start of immunosuppression to avoid the risk of disseminated disease.
- Generally avoid in immunosuppressed patients.
- When benefits of vaccination outweigh risk of discontinuing immunosuppressive medications:
 - Stop medications ≥ 4 weeks prior to live vaccine administration and continue to hold for 4 weeks afterward.

Timing of Vaccination With Inactive Vaccines

- Ideally complete any needed series > 2 weeks before immunosuppressive medications are started
- While on immunosuppressives:
 - Give as soon as possible and ideally during periods when immunosuppression is low
 - Some protection is better than none!
- Exception: B cell depleting biologics (e.g. rituximab RTX)
 - Administer at least 6 months after the start and 4 weeks before the next course when possible

Inactive Vaccines

- Influenza shot
- Pneumococcal
 - PPSV23
 - PCV13
- Hepatitis A
- Hepatitis B
- HPV
- Tetanus Toxoid



Influenza Vaccine

- Everyone gets a yearly **shot**
- Relatively unaffected by most DMARDs
- RTX can cause decreased efficacy – try to give vaccine prior to RTX or as long after RTX as possible
- Some protection better than none!

Pneumococcal Vaccines

- PCV-13 and PPSV-23 recommended
- Efficacy:
 - Anti-TNFs/TCZ have little/no effect on PPSV-23
 - RTX/tofa/MTX negatively affect response to PPSV-23
 - No data on Rheum meds + PCV-13
- Very important in patients with lupus nephritis
- Some protection better than none!

Hepatitis A and/or B

- Recommended for any non-immune adult who is at risk or requests it
- “At risk”: contact w/HBsAg+, >1 sexual partner in last 6 months, STD, MSM, IVDU, resident/staff MRDD, healthcare workers, ESRD, travelers to endemic areas, liver disease, DM, HIV
- Impact of DMARDs unknown; ?anti-TNF may humoral response

- 4-6 weeks after completing Hepatitis B vaccine series check an antibody titer to ensure that Hep B surface antibody seroconversion occurred
 - Anti-TNFs and SLE blunt immune response to HBV
 - Failure to seroconvert → may need to repeat the series

Tdap, Td, Meningococcal Vaccines

- Give per the same indications and schedules as the general adult population.
- Exception:
 - In the case of major and/or contaminated wound, patients (adult or pediatric) with RTX in the last 6mo should receive passive immunization with tetanus immunoglobulins.

HPV

- Recommended up to age 45 in some cases (used to be age 26)
- Burden of disease higher in women with RA (even w/o meds) and SLE
- Immunogenicity data limited – seems to be effective
- **Caution:** venous thromboembolic events have been reported with quadrivalent HPV vaccine, mostly in patients with antiphospholipid syndrome

Shingles Vaccine – NOT LIVE (RZV/Shingrix)

- “No recommendation”
- Unknown if affected by DMARDs or bDMARDs
- Case reports – no major problems
- Contains a novel adjuvant, associated with high reactogenicity rates in healthy adults, leading to concern it could worsen RD

Live Vaccines

- Herpes Zoster-Zostavax
- Measles, Mumps, Rubella (MMR)
- Yellow Fever
- Varicella
- Intra-nasal influenza
- Rotavirus
- Oral Polio
- Oral Typhoid
- Some formulations of Japanese encephalitis vaccine

Herpes Zoster (Shingles) Vaccine – LIVE (ZVL/Zostavax)

- 50+ and on traditional DMARDs and/or low-moderate GC – ok to give live vaccine
 - Efficacy relatively unaffected by DMARDs
- **Not** ok to give while on biologics
 - Risk of virus dissemination
 - No clear consensus on when live zoster vaccine can be given following biologics

- JAK inhibitors: safety signal for shingles
- Any patient who does not have documented shingles vaccine AND is starting a JAK inhibitor:
 - Consider testing VZV IgG
 - If negative, give VARICELLA VACCINE (2 doses, 28 days apart) prior to immunosuppression
- Patients born after 1980 – complicated
 - Vaccine records
 - Labs

MMR & Yellow Fever Vaccines

- Vaccination Possible:
 - Low-dose systemic or topical corticosteroids
 - Sulfasalazine
 - Hydroxychloroquine
 - Methotrexate <20mg/wk
- Vaccination Contraindicated:
 - Methotrexate >20mg/wk
 - Azathioprine
 - 6-mercaptopurine
 - All biologics

All Other Live Vaccines

- Generally avoid in immunosuppressed patients.
- When benefits of vaccination outweigh risk of discontinuing immunosuppressive medications:
 - Stop medications ≥ 4 weeks prior to live vaccine administration and continue to hold for 4 weeks afterward

Pediatric Patients With RD

- Inactive vaccines are generally considered safe in pediatric RD population and should be administered as per the national guidelines.
- Generally, live vaccines contraindicated while on immunosuppressive medications.

- Tetanus immunoglobulin advised in patients with contaminated wound in whom rituximab was administered in the last 6 months.

- Determination of pathogen-specific antibody concentration is recommended after vaccination in the following pediatric patients:
 - On Rituxan or high dose steroids:
 - Pneumococcus, influenza, and tetanus vaccines
 - On methotrexate:
 - PPV23

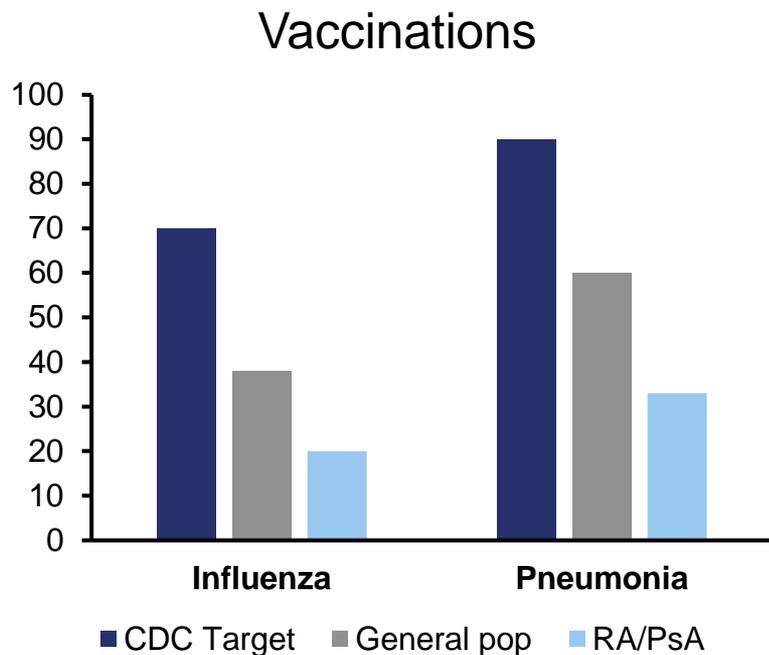
Special Circumstances

- Splenectomy or Hyposplenism
 - Susceptible to infections with capsulate microorganisms
 - Meningococcal, pneumococcal, influenza, H influenza B (HIB) vaccinations are advised

Special Circumstances Cont.

- Vaccination of Close Contacts of patients with RD
 - Immunocompetent household members should receive vaccines according to national guidelines
 - Exceptions:
 - Oral polio vaccines
 - Small risk of transmission to household members
 - Small risk of vaccine associated paralytic poliomyelitis in immunosuppressed household members
 - Avoid live vaccines for the first 6 months of life in newborns of mothers treated with biologics during the 2nd half of pregnancy

Increasing Vaccination Rates in RD Patients



- The strongest recommendations from literature review:
 - Use a team-based approach¹
 - Streamline workflow²
 - Utilize orders attached to an alert in the EMR³

¹Garg S, et al. 2018; Harris, et al. 2015;² Desai S.P., et al. 2013; Garg S. et al. 2016; Sheth, et al. 2017;

³Baker, et al. 2016; Karr, et al. 2016; Ledwich, et al. 2009; Sheth, et al. 2017.

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Questions?