

Welcome!

Thank you for joining us!
The webinar will begin shortly.





IDF's Mission

Improving the diagnosis, treatment and quality of life of people affected by primary immunodeficiency through a community empowered by advocacy, education and research.



Housekeeping



Zoom Webinars

Attendees will not have access to their mic or webcam throughout the event.



Slides

To see the full slides, select "side-by-side" in the dropdown menu at the top of your Zoom screen.



Questions

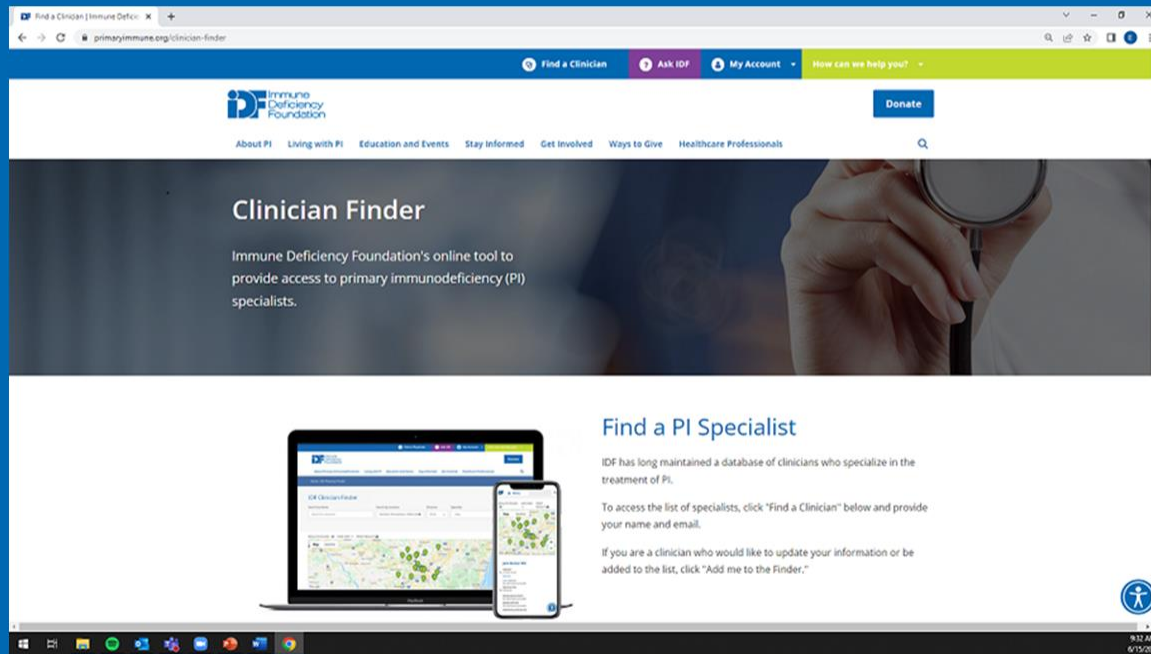
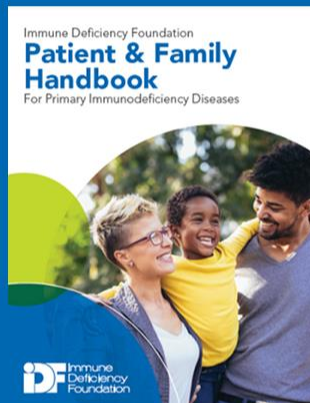
Submit your questions throughout the session via the Q&A Box.

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Connect & Collaborate



Monthly Lunch & Learns

Medical experts provide education on various diagnosis-specific topics.



IDF Webinars

Top Clinicians present on medical and lifestyle topics most pressing to the PI Community.



Get Connected Groups

Individuals and families living with PI can connect with others in their local community or online.



ASK IDF

Submit your questions about insurance, treatment options and more!



Annual PI Conference

Attend presentations from top immunology experts and engage with others in the PI Community.

WALK FOR PI 2023

Presented by



WALK FOR PRIMARY
IMMUNODEFICIENCY

Philadelphia, PA: July 15
Charlotte, NC: July 29
Milwaukee, WI: August 05
San Francisco, CA: August 19
Boston, MA: September 09
St. Louis, MO: September 23
Tampa, FL: October 07
Dallas, TX: October 21

Or join our virtual Walk:
Coast to Coast: December 02

#WalkForPI
www.walkforpi.org



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WELCOME!

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Prophylactic Antibiotics for Patients with Immunodeficiency

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Should Prophylactic Antibiotics be used in Primary Antibody Immune Deficiency?

What do we know?

Prophylactic Antibiotics in PI

- Currently, antibiotic prophylaxis is guided by the common pathogens seen in specific immunodeficiencies
- Experience with other chronic illnesses, eg. Cystic fibrosis, HIV, COPD, etc

Use of Prophylactic Antibiotics in Primary Immune Deficiency – Neutrophil Defects

- Chronic granulomatous disease
 - Typical pathogens are: *Staphylococcus aureus*, *Nocardia* species, *Serratia*, *Burkholderia cepacia*, and *Aspergillus*
 - Prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX)*
 - Autosomal CGD - resulted in the decreased incidence of nonfungal infections from 7.1 to 2.4 per 100 patient-months
 - X-linked CGD – 15.8 to 6.9 infections per 100 patient-months
 - No significant changes in the incidence of fungal infections
 - Itraconazole prophylaxis for fungal infections
 - Voriconazole and Posaconazole prevent invasive fungal infections
 - Toxicities – photosensitivity and hepatotoxicity (former) liquid formulation (latter)
 - Interferon gamma
 - Stimulated the oxidative burst up to 8-fold
 - Approximately two-thirds of patients with CGD, regardless of genetic defect
 - *enhance bactericidal activity*
- Margolis DM et al J Infect Dis, 1990
- Gallin J et al New Eng J Med 348:2416, 2003
- Slack MA and Thomsen IP J Ped Infect Disease 2018

Use of Prophylactic Antibiotics in Primary Immune Deficiency

- T-cell immune deficiency - SCID
 - Prophylaxis for opportunistic pathogens
 - *Pneumocystis jirovecii*
 - TMP-SMX
 - Viral and fungal infections
 - Fluconazole/ acyclovir
 - Avoid live viral vaccines
 - Breast milk may transmit CMV

Humoral immune deficiencies

- Encapsulated bacteria –
 - *Streptococcus pneumoniae*, *Hemophilus influenza*
- Use of prophylactic antibiotics varies widely

What do we know?

Lack of Controlled Studies

Nothing

Nada

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Niente

Rien

Ничего

Τίποτα

Use of Adjunct Prophylactic Antibiotics

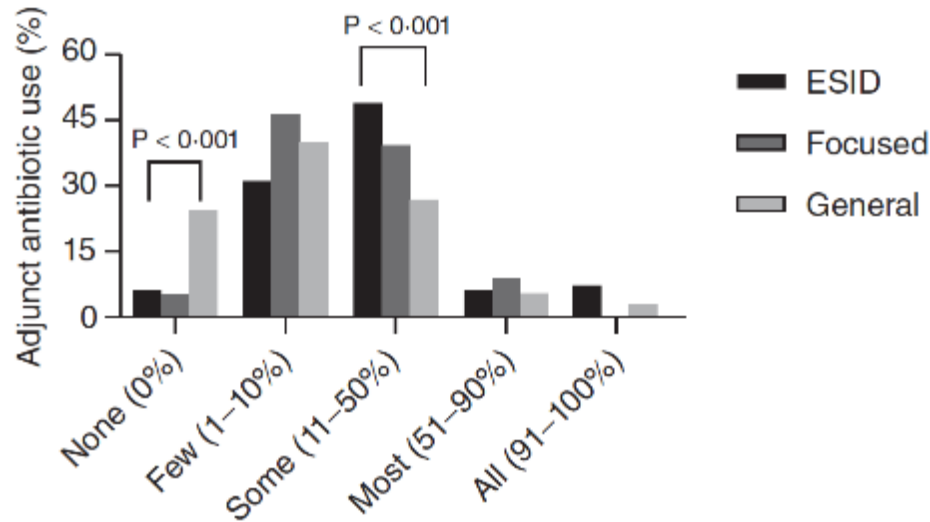
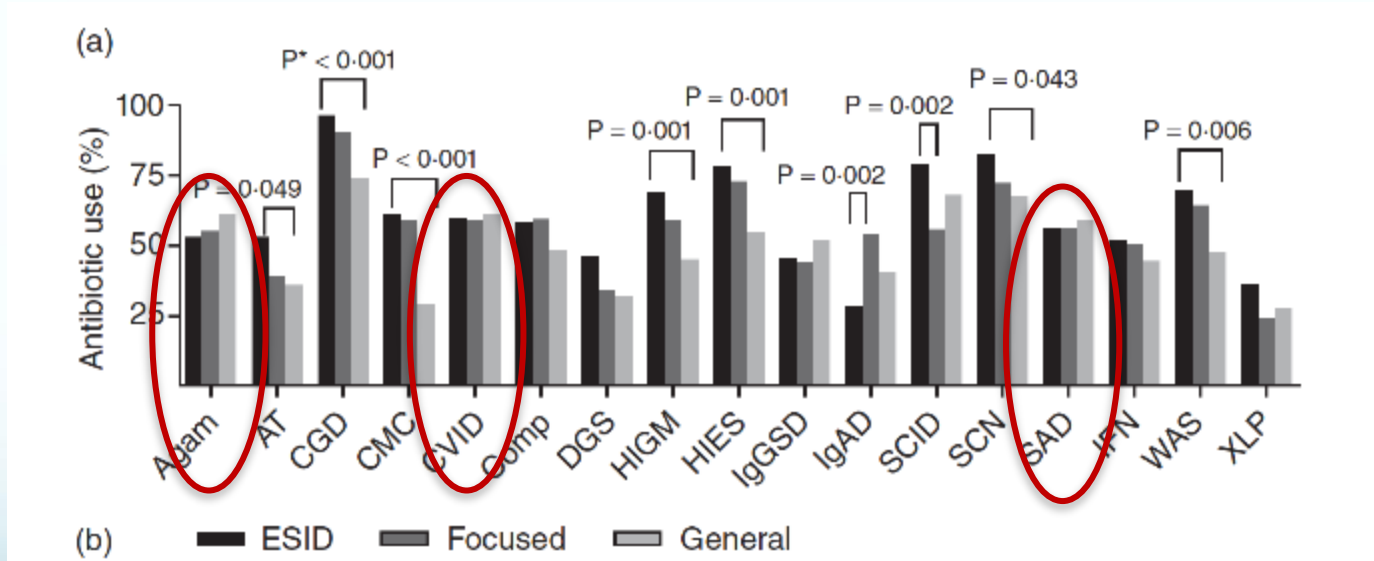


Fig. 4. Use of adjunct prophylactic antibiotics in primary immunodeficiency diseases (PIDs). Percentage of immunologists

Perceived Utility of Prophylactic Antibiotics in PID



Hernandez-Trujillo et al Clin & Exper Immunol, 2012

PEER PRESSURE!

Antibiotic prophylactic regimens in diseases with recurrent infections

Disease process	Regimens studied	Reference no.
Recurrent AOM	Amoxicillin 20 mg/kg once or twice daily, 6 mo	4, 5
	Sulfisoxazole 50 mg/kg/d, 6 mo	5
Chronic sinusitis	Erythromycin 250-500 mg twice daily, 12 wk	8
	Roxithromycin 150 mg daily, 12 wk	9
	Azithromycin 500 mg weekly, 8-20 wk	10
CF bronchiectasis	Azithromycin 500 mg 3 times a wk, 6 mo	15, 16
Non-CF bronchiectasis	Azithromycin 250 mg 3 times a wk, >3 mo	20
	Erythromycin 250 mg daily, 12 mo	21
	Azithromycin 500 mg 3 times a wk, 6 mo	22
	Azithromycin 250 mg daily, 12 mo	23

Kuruville M and de la Morena T
J Allergy Clin Immunol Pract 2013;1:573-82

Antibiotic prophylaxis regimens in primary antibody deficiency

PAD	Regimen
XLA or CVID (>3 breakthrough infections or extremely severe infection on IgG)	Azithromycin 5 mg/kg PO 3/wk (alternate days) or 10 mg/kg/wk; SMX-TMP 5 mg/kg TMP component PO daily or 3/wk
THI and selective IgA deficiency (seasonal intermittent during winter or continuous prophylaxis)	Azithromycin 5 mg/kg PO 3/wk or 10 mg/kg/wk; amoxicillin 20 mg/kg PO once or twice daily; SMX-TMP 5 mg/kg TMP component PO daily or 3/wk

PO, By mouth.

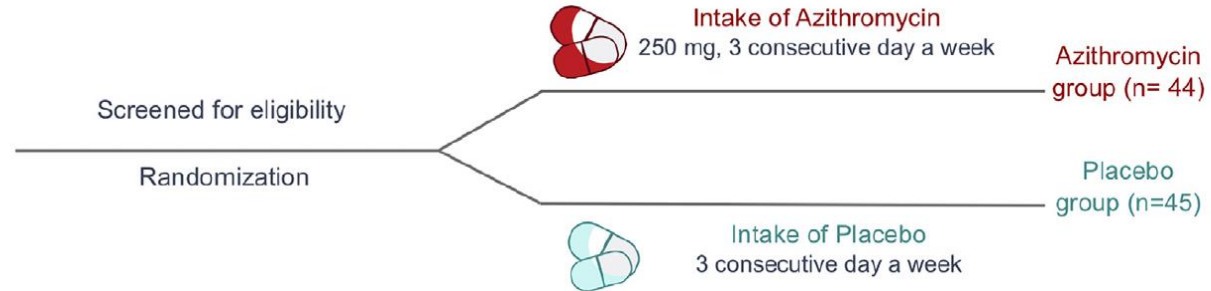
Selective Antibody Deficiency

- Prophylaxis antibiotics (PA) vs. Ig replacement therapy
 - Prospective cross over study (Netherlands) of 64 patients
 - The overall efficacy of the two regimens did not differ
 - A smaller proportion of patients suffered a related adverse event while using PA (26.8% vs. 60.3%, $p < 0.0003$, chi-squared test).
 - Patients with persistent infections while using PA suffered fewer infections per year after switching to IRT (2.63 vs. 0.64, $p < 0.01$).
- Conclusion: comparable efficacy of IRT and PA in patients with SAD Patients with persistent infections during treatment with PA had less infections after switching to IRT



DOUBLE-BLIND, PLACEBO-CONTROLLED RANDOMIZED TRIAL ON LOW DOSE AZITHROMYCIN PROPHYLAXIS IN PRIMARY ANTIBODY DEFICIENCIES

PAD adults with chronic infection-related pulmonary diseases (COPD, bronchiectasis, asthma) receiving treatment with IgRT.

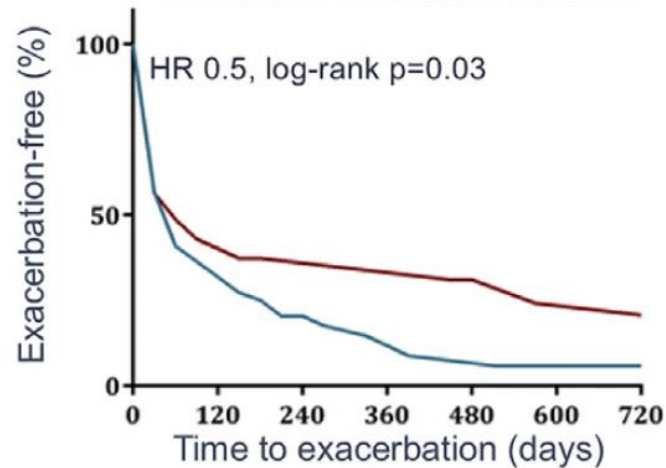


3-year, double-blind, placebo controlled, randomized clinical trial to test whether oral azithromycin (250 mg administered once daily 3 times a week for 2 years) would reduce respiratory exacerbations in patients with PADs and chronic infection–related pulmonary diseases.

COPD chronic obstructive pulmonary disease
HRQoL Health Related Quality of Life
FEV1 Forced Expiratory Volume 1st sec
IgRT Immunoglobulin Replacement Treatment
PAD Primary Antibody Defect

Primary outcome

In the **Azithromycin** group
lower risk for exacerbations



Secondary outcomes

In the **Azithromycin** group:

- Lower risk for hospitalization
- Lower need for additional antibiotic courses
- No higher rate of macrolides resistant-carriage
- No drug-related toxicity
- Improved HRQoL
- No effect on FEV1
- Reduced count in blood of neutrophils

Other PIs

- Hyper IgM deficiency –
 - Similar infections as XLA and CVID but CD40L def is a partial T-cell defect –
 - CD40L deficiency T cell defects predispose to *Pneumocystis jiroveci* (PCP), *Cytomegalovirus* (CMV), *toxoplasmosis*, *cryptosporidiosis* and sclerosing cholangitis
 - PCP prophylaxis with TMP-SMX

Risks of Prophylactic Antibiotic Use

Deaths From Drug-Resistant Infections Set To Skyrocket

Deaths from antimicrobial resistant infections and other causes in 2050

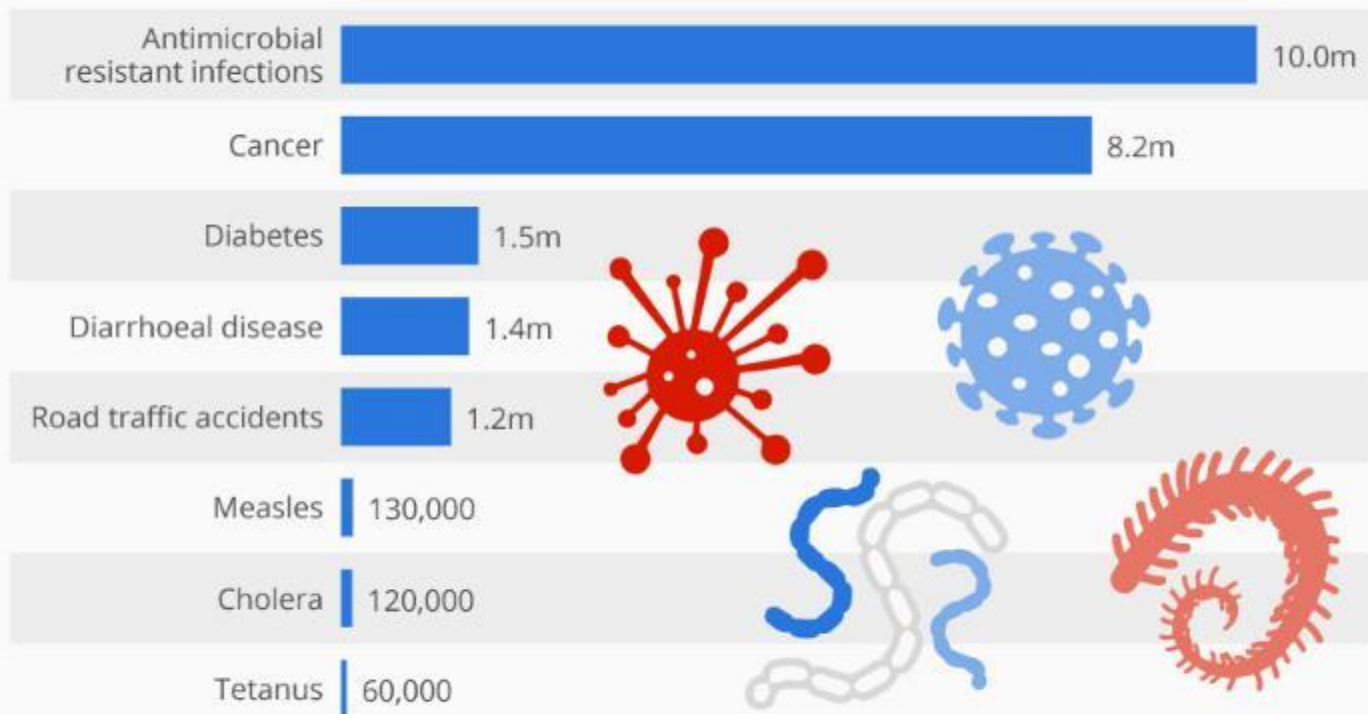
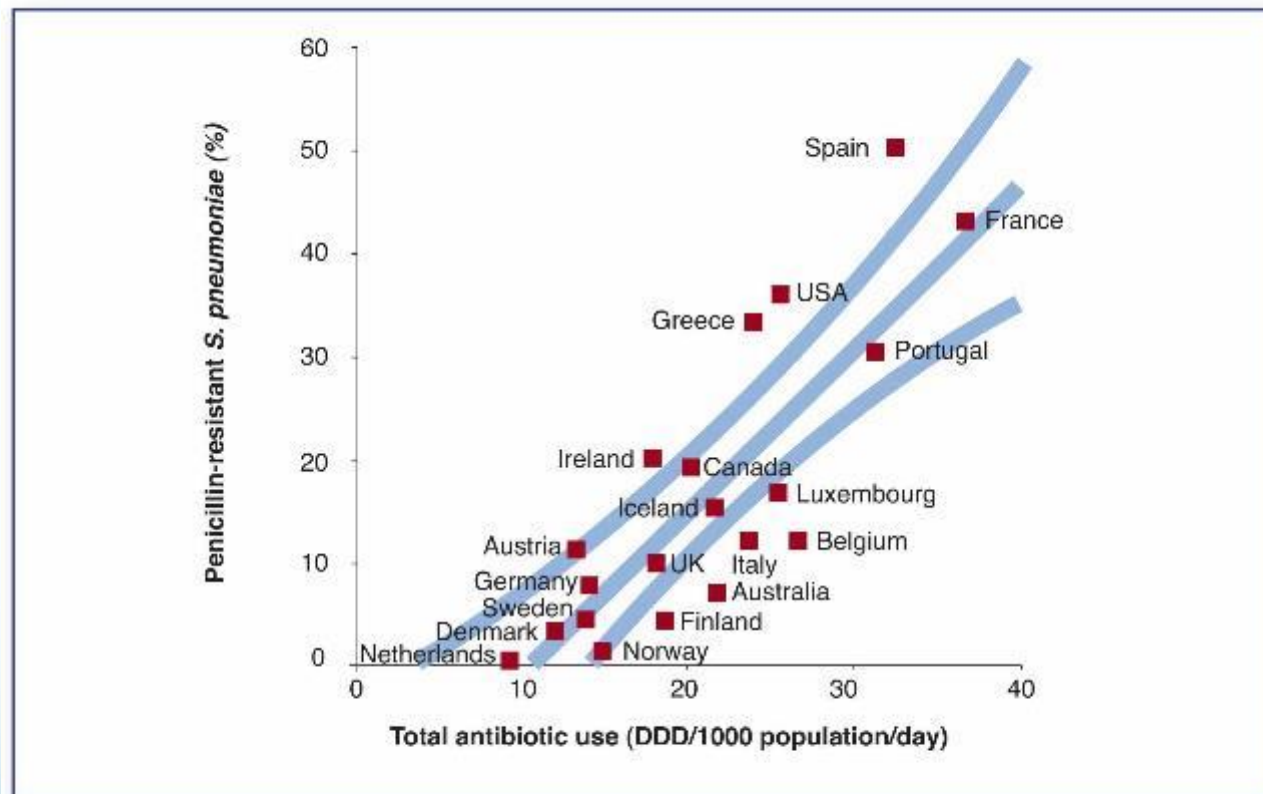


Figure 2.6 Antibiotic use and AMR from 1990–2000 in selected countries



DDD: Defined Daily Doses

Total antibiotic use in outpatients versus prevalence of penicillin-nonsusceptible *Streptococcus pneumoniae* in 20 industrialized countries.

Source: Reproduced from ⁸¹ with permission.

Bacteria and Fungi Listed in the 2019 AR Threats Report

Urgent Threats

- [Carbapenem-resistant *Acinetobacter*](#)
- [*Candida auris*](#)
- [*Clostridioides difficile*](#)
- [Carbapenem-resistant Enterobacterales](#)
- [Drug-resistant *Neisseria gonorrhoeae*](#)

Serious Threats

- [Drug-resistant *Campylobacter*](#)
- [Drug-resistant *Candida*](#)
- [ESBL-producing Enterobacterales](#)
- [Vancomycin-resistant *Enterococci* \(VRE\)](#)
- [Multidrug-resistant *Pseudomonas aeruginosa*](#)
- [Drug-resistant nontyphoidal *Salmonella*](#)
- [Drug-resistant *Salmonella* serotype Typhi](#)
- [Drug-resistant *Shigella*](#)
- [Methicillin-resistant *Staphylococcus aureus* \(MRSA\)](#)
- [Drug-resistant *Streptococcus pneumoniae*](#)
- [Drug-resistant Tuberculosis](#)

Concerning Threats

- [Erythromycin-Resistant Group A *Streptococcus*](#)
- [Clindamycin-resistant Group B *Streptococcus*](#)

Watch List

- [Azole-resistant *Aspergillus fumigatus*](#)
- [Drug-resistant *Mycoplasma genitalium*](#)
- [Drug-resistant *Bordetella pertussis*](#)

Key Concepts on the Use of prophylactic Antibiotics in Patients with PI

- Patients with chronic granulomatous disease benefit from prophylactic antibiotics, antifungals, and possibly interferon-gamma
- There are no published controlled studies of the benefits of antibiotic prophylaxis in patients with antibody immune deficiency diseases
- Microbial antibiotic resistance is a significant problem with the use of long term prophylactic antibiotic use, especially for macrolides
- Although it may be a common practice to "rotate" or periodically change antibiotics to avoid the development of resistance to a specific drug, studies have not been performed to compare rotation strategies



Q & A

THANK YOU!

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From all of us at IDF

Thank You!

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You make the IDF community stronger