

Role of Vaccines in National Strategies to Combat Antibiotic-Resistant Bacteria

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NVAC

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Timeline of Federal Efforts in Support of National Strategies to Combat Antibiotic Resistant Bacteria

President's National Strategy for Combating Antibiotic resistant Bacteria (CARB)–
September 18, 2014

President's Proposed Budget to fund antibiotic resistance efforts across the government in FY 2016 -
January 27, 2015



President's Council of Advisors on Science and Technology (PCAST) report Combating Antibiotic Resistance to the President - **September 18, 2014**

Executive Order 13676 Combating Antibiotic Resistant Bacteria – (CARB)–
September 18, 2014

National Action Plan to Combat Antibiotic Resistant Bacteria (CARB)–
March 27, 2015



CARB Working Groups



HHS CARB Advisory Committee Inaugural meeting expected
Summer/Fall 2015

CARB Strategy and Action Plan

GOALS:

- 1) Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections
- 2) Strengthen National One-Health Surveillance Efforts to Combat Resistance
- 3) Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria
- 4) Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines
- 5) Improve International Collaboration and Capacities for Antibiotic-resistance Prevention, Surveillance, Control, and Antibiotic Research and Development

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Preventing Infections, Preventing Spread of Antibiotic Resistance- Role of Vaccines in Fostering Antibiotic Stewardship

1) Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

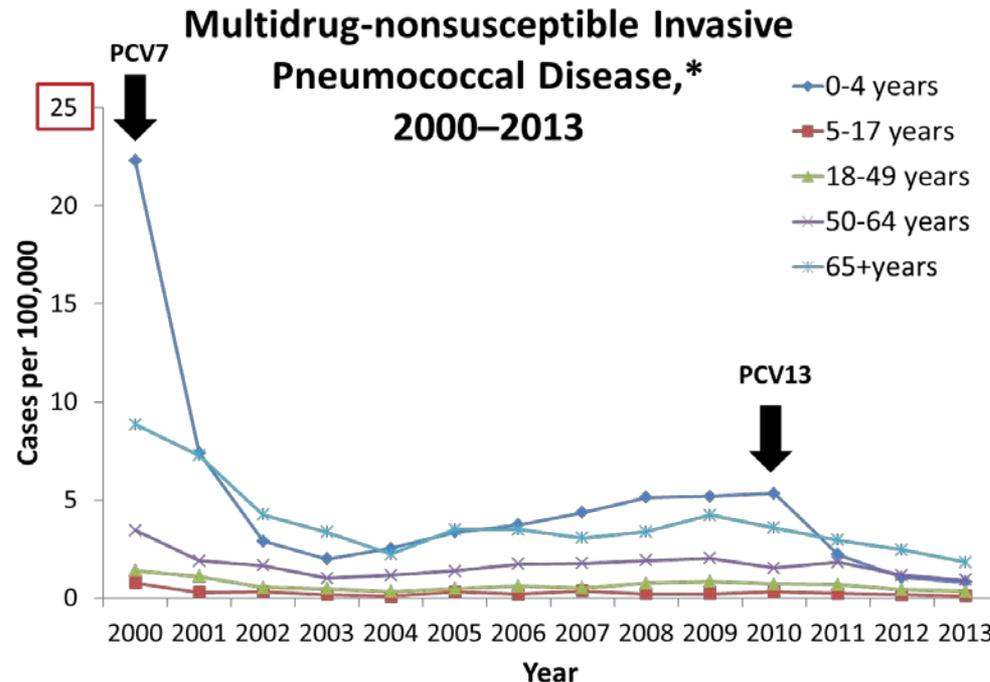
- Vaccines prevent disease, decreasing the need for antibiotic use

<i>Haemophilus influenzae</i> Type b (Hib) Conjugate Vaccine	Pneumococcal Conjugate Vaccines (PCV7, PCV13)	Influenza Vaccine
<ul style="list-style-type: none"> • Prior to vaccine introduction, ~20,000 cases of invasive Hib disease in children <5years 	<ul style="list-style-type: none"> • Within 7 years of introduction of PCV7, rates of PC7-type IPD in children < 5years dropped from 80 cases per 100,000 to less than 1 case per 100,000. 	<ul style="list-style-type: none"> • 5-20% of population infected each year
<ul style="list-style-type: none"> • Widespread use of vaccine in children decreased incidence of invasive Hib disease by 99% 	<ul style="list-style-type: none"> • 2003 – PCV7 uptake estimated to prevent 1.4 million antibiotic prescriptions annually (<i>Fireman et al, 2003</i>) 	<ul style="list-style-type: none"> • Inappropriate antibiotic use for treating influenza patients found to be as high as 79% (<i>Misurski et al, 2011</i>)
<ul style="list-style-type: none"> • Vaccination decreases bacterial carriage 	<ul style="list-style-type: none"> • Vaccination decreases bacterial carriage • Disease reduction in all populations due to community protection • Increased uptake of PVC13 in adults will magnify benefits. 	<ul style="list-style-type: none"> • Influenza-associated antibiotic prescriptions decreased 64% following universal vaccination recommendation in Canada (<i>Kwong et al, 2009</i>)

Preventing Infections, Preventing Spread of Antibiotic Resistance- Role of Vaccines in Fostering Antibiotic Stewardship

1) Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

- Vaccines prevent disease, decreasing the need for antibiotic use
- Current vaccines against bacterial pathogens have already demonstrated benefits in reducing transmission of antibiotic resistant strains in the population



Source: ABCs, unpublished data, 2014.

*Defined as nonsusceptible to ≥ 3 antibiotic classes.

Preventing Infections, Preventing Spread of Antibiotic Resistance- Role of Vaccines in Fostering Antibiotic Stewardship

1) Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

- Vaccines prevent disease, decreasing the need for antibiotic use (both appropriate and inappropriate)
 - Use of antibiotics drives antibiotic resistance
- Current vaccines against bacterial pathogens have already demonstrated benefits in reducing transmission of antibiotic resistant strains in the population
- Vaccines also decrease unnecessary interactions with the healthcare system
 - Fewer opportunities for colonization and infection with healthcare associated pathogens

Preventing Infections, Preventing Spread of Antibiotic Resistance- Role of Vaccines in Fostering Antibiotic Stewardship

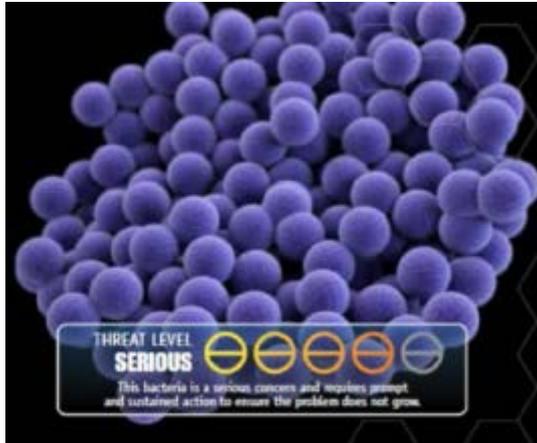
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Antibiotic stewardship efforts are strengthened by advocating for increased vaccine uptake in communities

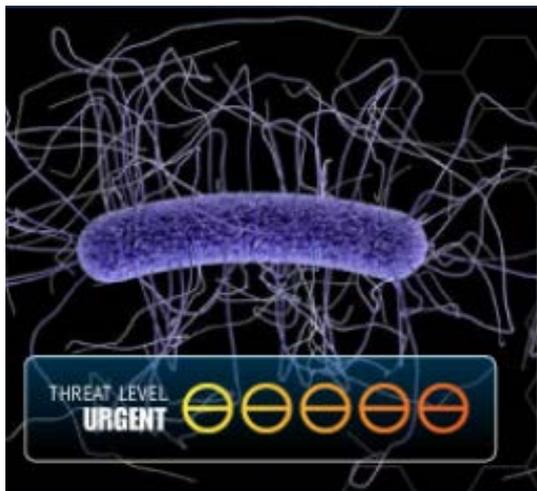
Supporting Long Term Solutions for Combating Antibiotic-Resistant Bacteria

4) Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines



Methicillin-resistant *Staphylococcus aureus* (MRSA)

- >80,000 severe infections, >11,000 deaths per year
- Community and healthcare- acquired infections
- Vaccine candidates being explored



Clostridium difficile

- 500,000 infections, 29,000 deaths per year
- Community and healthcare-acquired infections
- Treatment often leads to further imbalance in gut microbiome
- Burden to healthcare system estimated \$1-3B; vaccines estimated to be cost-effective and cost-saving solution
- Vaccine candidates currently in Phase III clinical trials

Identifying Economic Incentives to Support Development of Vaccines Against Antibiotic-Resistant Bacteria

4) Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines

Objective 4.5 Expand ongoing efforts to provide key data and materials to support the development of promising antibacterial drug candidates and promising vaccines that can reduce the need to treat bacterial infections

Will the economic incentives described for antibiotics work for vaccines?



Recommendations

Role of vaccine stakeholders in antibiotic stewardship efforts

Recommendation 1:

The National Vaccine Advisory Committee (NVAC) recommends that the Assistant Secretary for Health (ASH), as the Director of the National Vaccine Program, work with HHS agencies and other federal and nonfederal partners to develop a stakeholder engagement plan to ensure vaccine and immunization and antimicrobial stewardship stakeholder efforts include information on the role of existing vaccines in minimizing antibiotic use. This should include information on vaccines against bacterial pathogens which may currently be or potentially become antibiotic resistant as well as viral vaccines that by preventing viral illnesses decrease the inappropriate use of antibiotics for viral infections as well as decrease bacterial superinfections leading to needs for antibiotics.

- These efforts should include a comprehensive analysis modeling the reduction in disease burden due to antibiotic resistant strains, the potential reduction in antibiotic prescribing and healthcare encounters, and the anticipated cost-savings to the healthcare system expected from increased uptake of recommended vaccines in all age groups. Vaccines under development may also be included to support vaccine development efforts.
- These efforts should also tie into surveillance efforts to determine the effects that vaccine uptake has produced on minimizing disease burden due to antibiotic resistant strains in all age groups, and on the ecology of infections caused by both vaccine and non-vaccine strains. When possible, surveillance efforts also should inform on the effects vaccine uptake, and the reduction in disease caused by vaccine, has had on the prevalence of antibiotic resistant strains.

Recommendations

Harmonizing Departmental Efforts and Expertise to Support Strategies for Combating Antibiotic Resistant Bacteria

Recommendation 2:

The NVAC strongly recommends that the ASH ensure NVAC remains regularly informed of efforts to address antibiotic resistance by revising the NVAC charter to include a liaison representative from the President's Advisory Council on Combating Antibiotic Resistant Bacteria on the NVAC. The NVAC also encourages the ASH to support the future inclusion of an NVAC representative on the President's Advisory Council on Combating Antibiotic Resistant Bacteria to provide knowledge of vaccines and the immunization system to their discussions. Cross representation on Committees maximizes the use of subject matter expertise and stakeholder input to better harmonize Departmental efforts.

Recommendations

Analysis of Economic Incentives Appropriate to Support Development of Promising Vaccine Candidates Targeting Antibiotic Resistant Pathogens

Recommendation 3

The NVAC strongly encourages the ASH to communicate to the HHS Secretary and the CARB Economic Incentives Working Group that incentives proposed to stimulate antibiotic development must also be evaluated for their utility to accelerate the development of vaccines and other novel prevention strategies. Proposed incentives must be flexible enough to apply to a range of diverse technologies to ensure that we continue to move towards long term solutions to antibiotic resistance. When incentives are not found to be cross-cutting, additional alternative incentives should be proposed and analyzed to promote a more robust and comprehensive pipeline that includes vaccines.

- Once appropriate economic incentives are identified, NVAC recommends that the ASH work with relevant federal and non-federal stakeholders to prioritize promising vaccine candidates to ensure programmatic resources support vaccine candidates with the greatest potential impact for combating antibiotic resistance and reducing the use of antibiotics in healthcare and community settings.

Recommendations

Collaboration to enhance early communication to identify appropriate regulatory pathways

Recommendation 4

The NVAC recommends that the ASH work with FDA and vaccine manufacturers (including pre-commercial stage biotechnology companies) to encourage early discussion of appropriate regulatory pathways and clinical trial design requirements for the development of vaccines targeting antibiotic-resistant bacteria, and vaccines that decrease the use of antibiotics.

Recommendations

Recommendation 5

**ADDED AS PART OF NVAC DISCUSSIONS
06/10/2015**

The NVAC requests that NVPO provide an annual update on the progress made in supporting the role of vaccines in strategies to combat antibiotic resistant bacteria

Acknowledgements

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