

VACCINES FOR GN HEALTHCARE PATHOGENS: NO ESKAPE

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**GLOBAL VACCINE AND IMMUNIZATION RESEARCH
FORUM: MARCH 15-17, 2016**

DISCLOSURES

- **Merck (speaker's bureau, consultant)**
- **Pfizer (speaker's bureau, consultant)**
- ***Roche (consultant)***
- **Genentech (Research Grant)**
- **Valneva (consultant, Research Grant)**
- **Ysios Investment Capital (consultant)**

Why



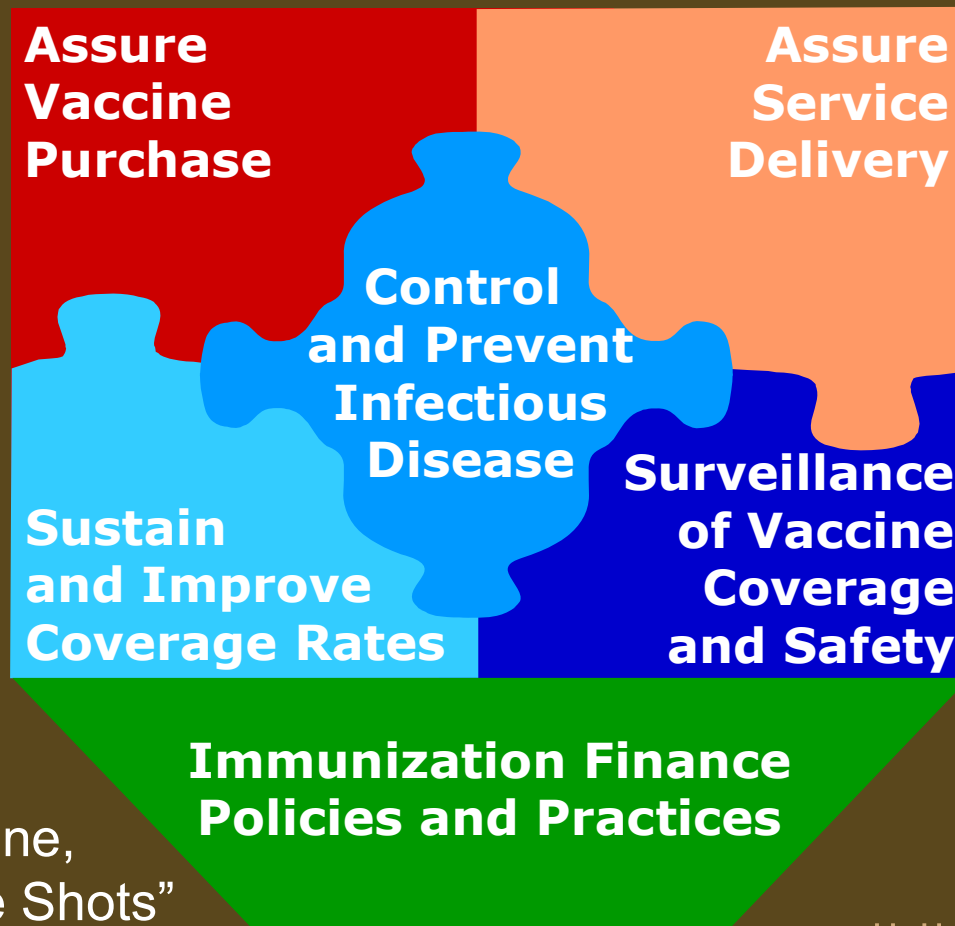
Edward Jenner, 1749-1823



Why ?

- **Why are we here?**
- **Why vaccines are in the Media?**
- **Why we need to look to vaccines for HCl (instead of just drugs)**
- **Why have been done?**
- **Why we don't have any vaccines for them now?**
- **Why this is a venture that will benefit patients, healthcare and companies?**

Six Roles of Immunization Programs



Institute of Medicine,
1999, "Calling the Shots"

provided by Lance Rodewald email, 9/24/08

GREATEST PUBLIC HEALTH ACHIEVEMENTS IN THE US

1900-1998

- **Vaccination**
- Motor vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline in deaths from coronary artery disease and stroke
- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water

2001-2010

- **Vaccination**
- Prevention and control of communicable diseases
- Tobacco control
- Maternal and infant health
- Motor vehicle safety
- Cardiovascular disease prevention
- Occupational safety
- Cancer prevention
- Childhood lead poisoning prevention

KEY REFERENCES & MEDIA


Centers for Disease Control and Prevention
MMWR Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 60 / No. 2 January 28, 2011

General Recommendations on Immunization
Recommendations of the Advisory Committee
on Immunization Practices (ACIP)



Centers for Disease Control and Prevention
MMWR Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 60 / No. 7 November 25, 2011

Immunization of Health-Care Personnel
Recommendations of the Advisory Committee on
Immunization Practices (ACIP)





RECOMMENDED ADULT IMMUNIZATION SCHEDULE: US, 2015

Figure 2. Vaccines that might be indicated for adults based on medical and other indications¹

VACCINE ▼	INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV]) ^{4,6,7,8,13}	HIV infection CD4+ T lymphocyte count ^{4,6,7,8,13}		Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies) ^{8,12}	Chronic liver disease	Diabetes	Healthcare personnel
				< 200 cells/ μ L	\geq 200 cells/ μ L							
Influenza ^{*2}			1 dose IIV annually			1 dose IIV or LAIV annually	1 dose IIV annually					1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap) ^{*3}	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs										
Varicella ^{*4}		Contraindicated		2 doses								
Human papillomavirus (HPV) Female ^{*5}		3 doses through age 26 yrs		3 doses through age 26 yrs								
Human papillomavirus (HPV) Male ^{*5}		3 doses through age 26 yrs		3 doses through age 21 yrs								
Zoster ⁶		Contraindicated		1 dose								
Measles, mumps, rubella (MMR) ^{*7}		Contraindicated		1 or 2 doses								
Pneumococcal 13-valent conjugate (PCV13) ^{*8}				1 dose								
Pneumococcal polysaccharide (PPSV23) ⁹				1 or 2 doses								
Meningococcal ^{*9}				1 or more doses								
Hepatitis A ^{*10}				2 doses								
Hepatitis B ^{*11}				3 doses								
<i>Haemophilus influenzae</i> type b (Hib) ^{*12}		post-HSCT recipients only		1 or 3 doses								

*Covered by the Vaccine Injury Compensation Program

 For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

 Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

 No recommendation

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BAD BUGS, NO DRUGS

As Antibiotic Discovery Stagnates ...
A Public Health Crisis Brews

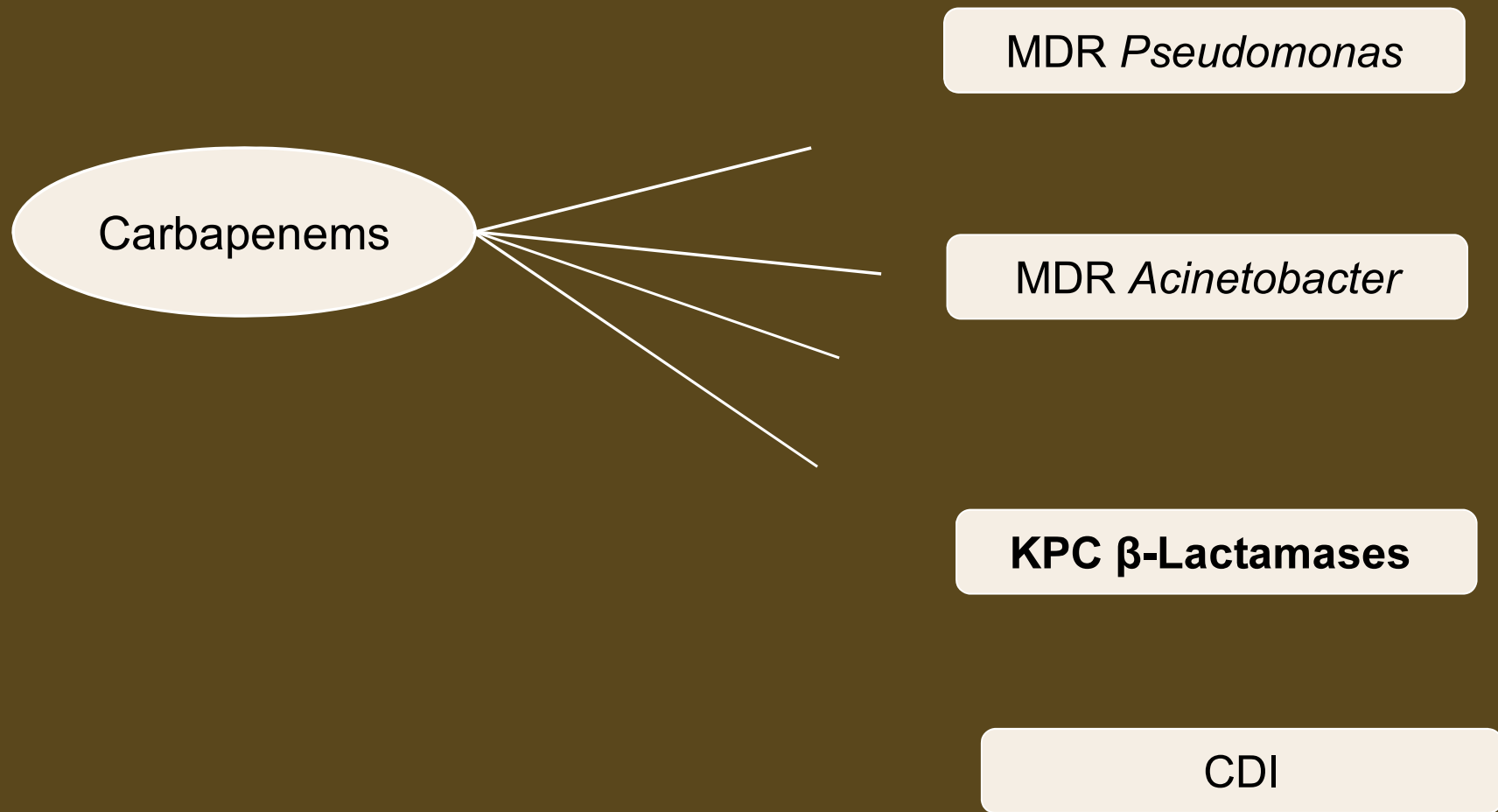


 **IDS**A
Infectious Diseases Society of America

July 2004

- **The widespread use of potent, broad-spectrum antibiotics has been paralleled by the development of resistance in bacteria**
- **It is thus necessary to search alternatives**

An Additional Point to Consider When Selecting Antimicrobial Coverage—Collateral Damage



Stewardship: One Goal ... Two Perspectives

Current Opinion in
Critical Care 

Volume 12(5), October 2006, p 452-457

De-escalation therapy in ventilator-associated pneumonia
Michael S. Niederman

Current Opinion in
Pulmonary Medicine 

Volume 12(5), September 2006, p 364-368

De-escalation in lower respiratory tract infections
Thiago Lisboa^a and Jordi Rello^b

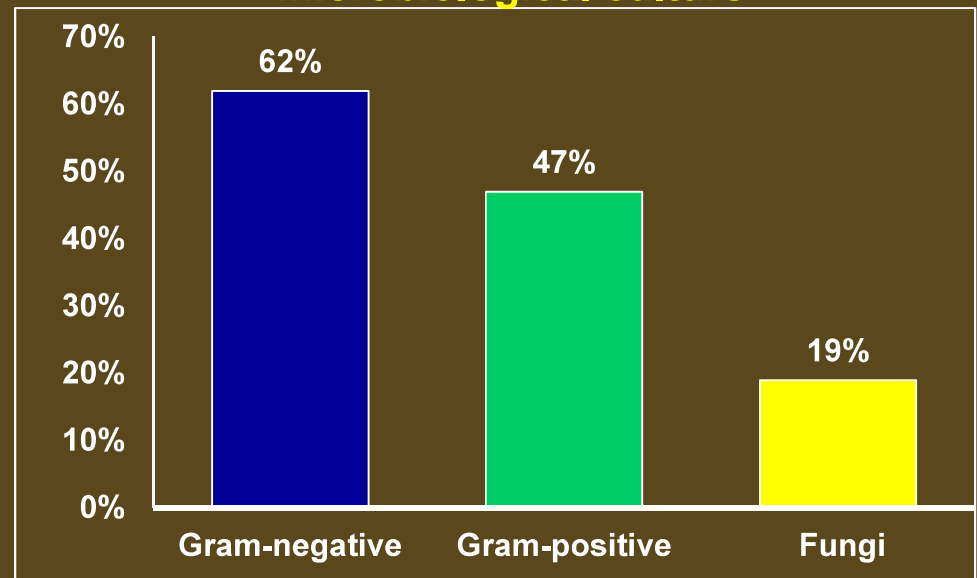
EPIC II – The Extended Prevalence of Infection in Intensive Care

1 day (May 8, 2007), prospective, 14 414 pt in 1 265 ICUs from 75 countries

64% RTI, 20% abdomen, 15% bloodstream, 14% RT/GUS

71% received antibiotics (prophylaxis or treatment)

Distribution of pathogen in all positive microbiological culture

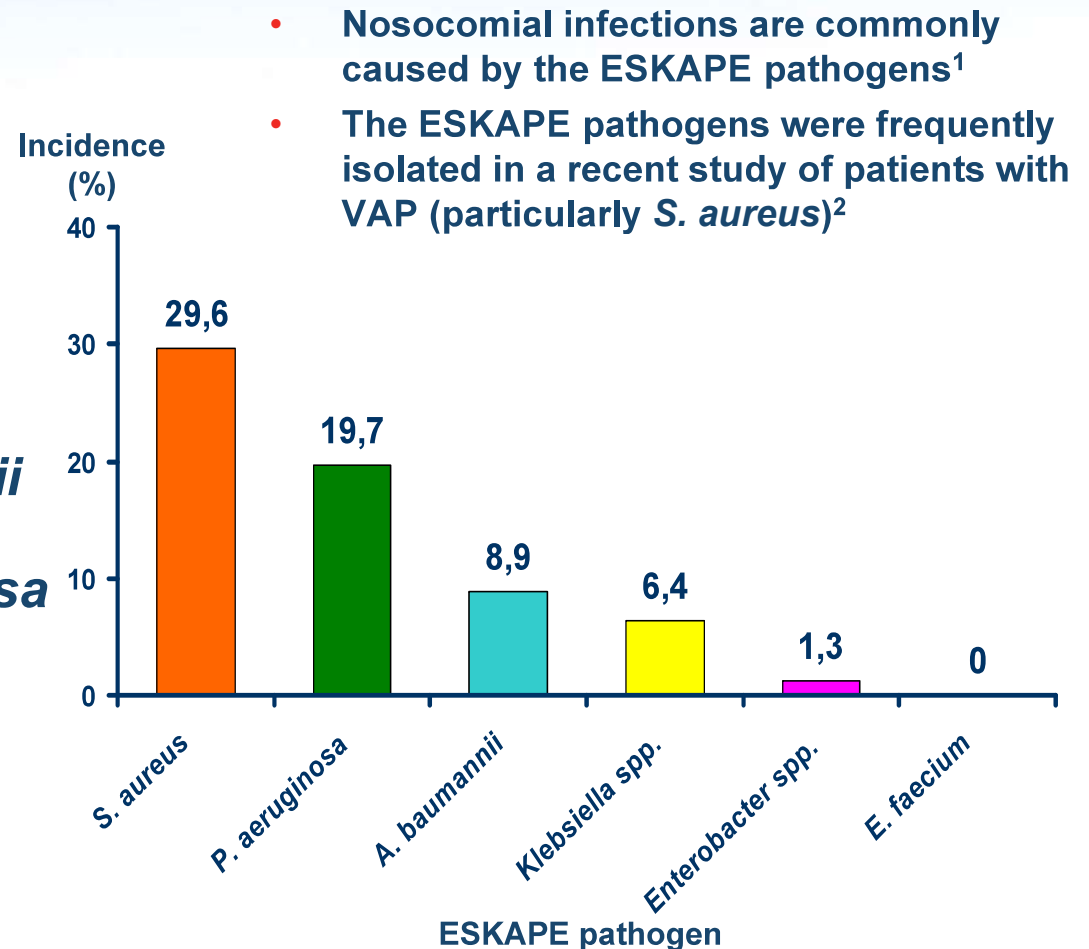


RTI –respiratory tract infection
RT renal tract
GUS –genitourinary system

J.-L. Vincent, J. Rello, et al. JAMA; 2009. 302:2323-2329

The ESKAPE pathogens and NP

E *Enterococcus faecium*
S *Staphylococcus aureus*
K *Klebsiella pneumoniae*
A *Acinetobacter baumannii*
P *Pseudomonas aeruginosa*
E Enterobacter



1. Rice. J Infect Dis 2008;197:1079-1081

2. Sandiumenge et al. Chest 2011;140:643-651

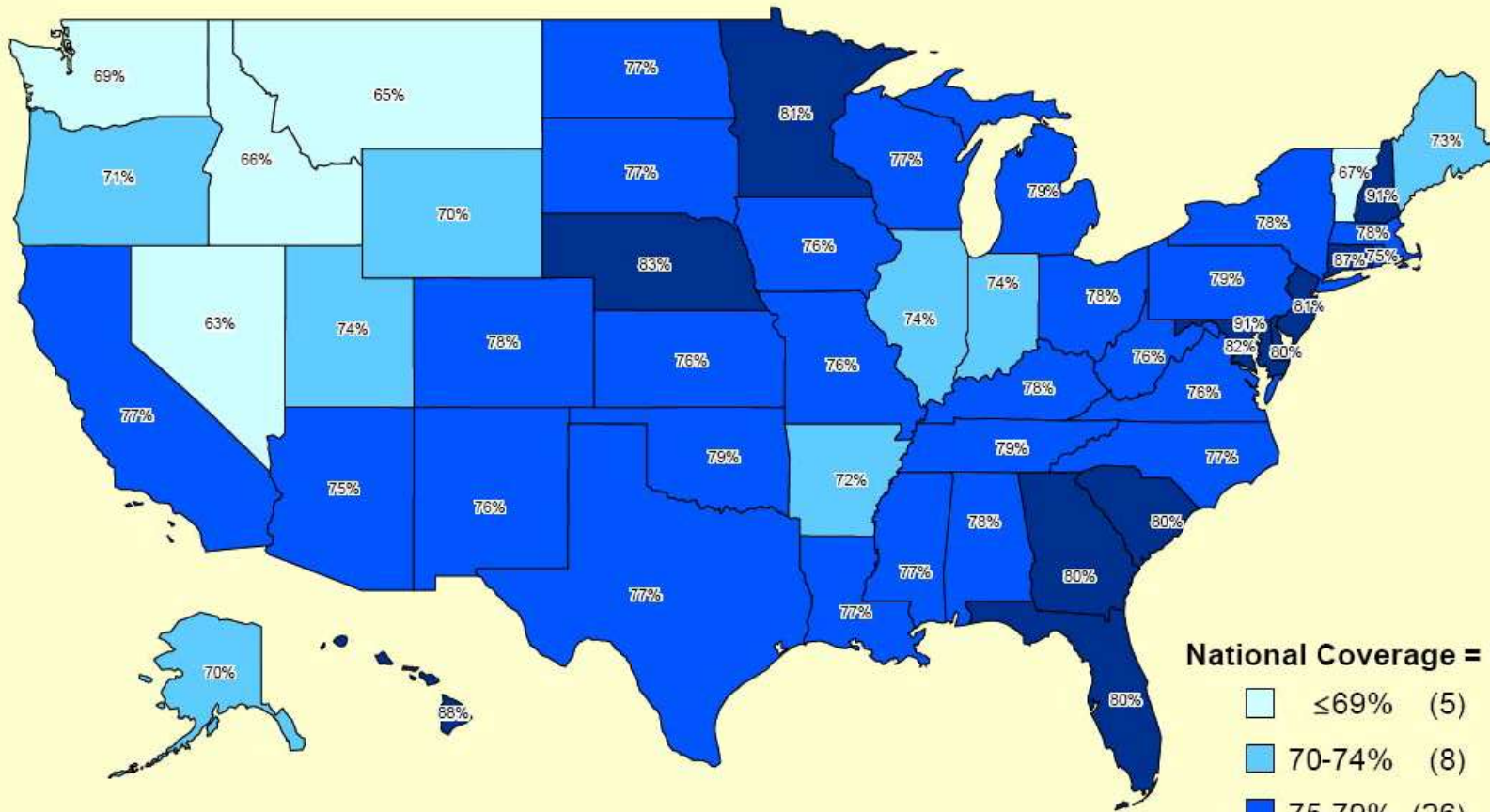
Why there are few new antibiotics over the past 30 years?

- **Economic: Expensive to develop**
- **Scientific-Research:**
 - Finding new sources is not easy**
 - Safety**
- **Regulatory: Difficult Process**
- **National & Hospital Barriers to Introduction**
- **New Emergence of Resistance**

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4:3:1:3:3:1* Series Coverage: Children 19-35 Months, 2007



National Coverage = 77%

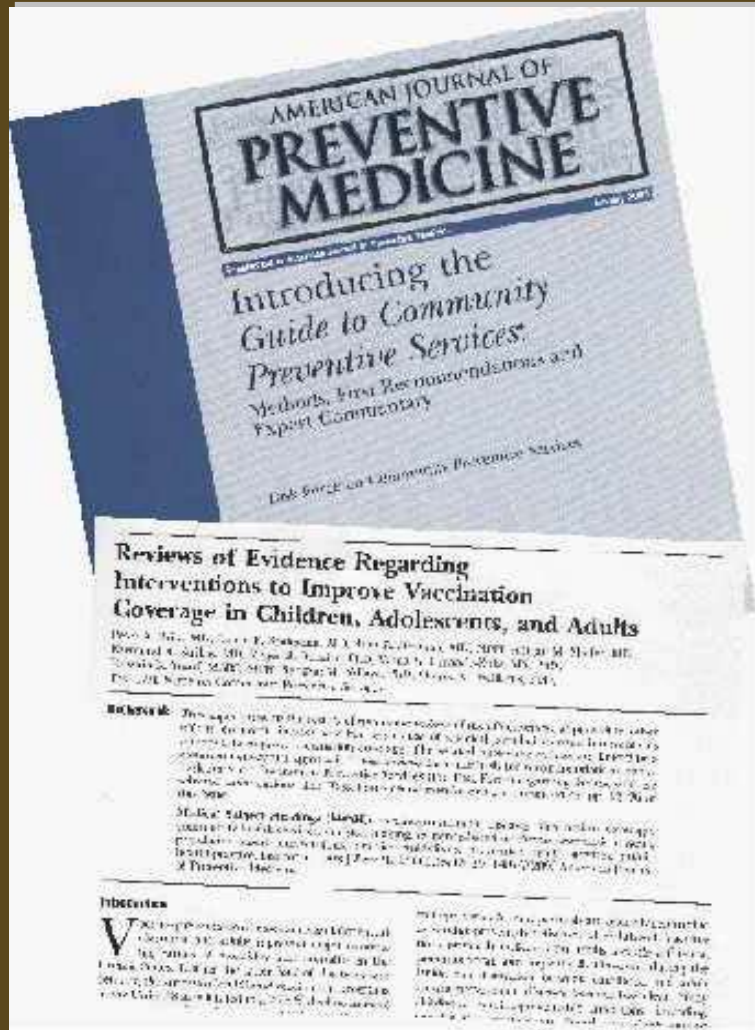
- ≤69% (5)
- 70-74% (8)
- 75-79% (26)
- ≥80% (12)

Note 1: *4+DTP, 3+Polio, 1+MMR, 3+Hib, 3+HepB, 1+Varicella.
 Note 2: Includes children born between January 2004 and July 2006
 Source: National Immunization Survey (NIS)



provided by Lance Rodewald email, 9/24/08

Published Evidence-Based Research



provided by Lance Rodewald email, 9/24/08

Failures in *P. aeruginosa* Vaccination

- **Octavalent O-polysaccharide-toxin A conjugate vaccine (Aerugen)**
- **bivalent flagella-based vaccine in cystic fibrosis**
- **hyperimmune globulin derived from donors immunized with an O-polysaccharide-toxin A-based vaccine in combination with a *Klebsiella* capsular polysaccharide vaccine**

Grimwood K et al. *Hum Vaccin Immunother.* 2015; 11: 14-20.

Other Projects: phase II IC43 (Valneva)

- **IC43: consist of a hybrid molecule of two of the outer membrane proteins of *Pseudomonas aeruginosa* (OprF and OprI).**
- **In a trial in mechanically ventilated patients all vaccine groups showed good rates of seroconversion at day 14 but there were no differences in the rates of *Pseudomonas aeruginosa* infection among the groups (two different doses with aluminium hydroxide-a adjunctive vaccine, a dose with non-adjunctive vaccine and placebo).**
- **The 28-day mortality was lower in all vaccine groups compared with the control group.**

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Concerns about ESKAPE Vaccine Initiatives

- **Physicians**
- **Manufacturers**
 - Federal contract covers too much of the market – a monopsony
 - Potential for future price controls
- **Public Health**
 - VFC does not cover enough of the population
 - Complex accountability
- **Private Providers**
 - Does not cover costs of administration
 - Does not cover many of their patients (e.g., underinsured)
 - Dual ordering system

Barriers to ESKAPE Vaccination

- **Economic Cost**
- **Safety Concerns**
- **Seroconversion Time**
- **Intervinable barriers**
 - **Clinicians believe coverage is higher than it is**
 - **Clinicians do not operate recall systems**
 - **Records are scattered across providers**
 - **Results**
 - *Complacency*
 - *Information gap*
 - *Missed immunization opportunities*

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Goals in Vaccine Policy Making

- **Global**
- **Multidisciplinary broad-based input from:**
 - infectious disease experts
 - pediatricians, family physicians, internists
 - regulators
 - public health experts
 - vaccine experts
 - consumers
 - manufacturers

The ACIP Process: Factors Considered in Recommendations

- Licensed indications and schedule
- Disease burden overall and in **risk groups**
- Data on safety and efficacy
- Feasibility in the context of existing recommendations
- Equity in access to vaccine and good use of public funds (cost effectiveness)
- Recommendations of other groups (e.g., AAP, AAFP)

Recommended Provider-Based Strategies

- **Assessment with feedback to providers**
- **Provider prompting**
- **Standing orders for adults**
- **Education coupled with other strategies**
- **Communication**

Financial Incentives

- **Entitlement**
- **Pre-emptive use pre-surgery**
- **High Global Market**
- **Allows multiple companies to compete**
- **No emergence of Resistance**
- **Value for Money**
- **Not seasonal**

Main Targets: Patients, Patients, Patients

- CF patients
- SOT patients
- BMT patients
- COPD
- Cancer Patients
- Surgery Patients at Risk of HCI
- **Mechanical Ventilated Patients**

Other Aspects of the Immunization System Not Covered in this Talk

- **Vaccine safety monitoring**
- **Inequity and risk communication**
- **Compensation programs**
- **Monoclonal Antibodies (mAB)**

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