

What Immunization Providers Need to Know about Vaccine Safety and Addressing Parental Concerns

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National Infant Immunization Week

April 2012

Overview of Presentation

- ❑ **How we assess vaccine safety in the United States**
- ❑ **Updates on several current vaccine safety issues**
- ❑ **What are parents concerned about, and how to address those concerns**

Disclosure

- ❑ No financial relationships to disclose**
- ❑ No discussion of investigational products or recommendations for off-label use of licensed vaccines**

What Immunization Providers Need to Know

HOW WE ASSESS VACCINE SAFETY IN THE UNITED STATES

The Vaccine Safety System

- ❑ **When the vaccine is under development, studies are done to find out if it is safe and effective**
- ❑ **FDA review: if safe and effective, vaccine can be licensed**
 - Other issues (manufacturing etc.) also considered by FDA
- ❑ **Ongoing monitoring by both CDC and FDA and by the manufacturer after licensure**
 - Post-licensure studies by the manufacturer
 - Vaccine Adverse Event Reporting System (VAERS)
 - Special studies
- ❑ **If vaccine safety issues are identified, actions are taken**

Vaccine Safety

❑ Surveillance

- Vaccine Adverse Event Reporting System

❑ Rapid studies

- Rapid cycle analysis through the Vaccine Safety Datalink

❑ Other special studies

- Guillain-Barré syndrome following H1N1 vaccine
- Vaccines and autism

❑ Prevention

- Contraindications and precautions for use of vaccines
- Withdrawal of recommendations for use of vaccines

Vaccine Adverse Event Reporting System

- ❑ National spontaneous reporting system for adverse events following immunization
- ❑ Jointly run by CDC and FDA
- ❑ VAERS has led to early identification of serious adverse events
- ❑ Limitations
 - Reporting is not complete
 - Rarely able to establish a causal relationship to vaccine based on reports to VAERS
- ❑ VAERS reports can be submitted online and data are publicly accessible:
<http://vaers.hhs.gov>

A Faster Approach to Vaccine Safety Studies

- ❑ **Alternative to traditional post-licensure vaccine safety study methods, which generally take years to complete**
- ❑ **The Rapid Cycle Analysis approach in the Vaccine Safety Datalink:**
 - Tests specific hypotheses with well-defined outcomes
 - Each week, evaluate the number of events in vaccinated persons
 - Compare it to the expected number of events based on a comparison group
 - Weekly analyses with statistical adjustment for multiple looks
- ❑ **Rapid Cycle Analyses have:**
 - Provided reassuring data on safety of several newly introduced vaccines (e.g., Rotateq, 2009 H1N1 vaccine)
 - Identified increased risk of febrile seizures following MMRV vaccine

Are Vaccines Safe?

- ❑ **Minor adverse events are common**
- ❑ **Serious adverse events that we know are caused by vaccines are not common**
 - Oral polio vaccine caused vaccine-associated polio in 1 out of 750,000 first doses
 - Influenza vaccine caused Guillain-Barré syndrome in 1 out of 100,000 doses (1976)
 - MMR causes thrombocytopenia in 1 out of 30,000 doses

Not Everything Bad that Happens after Vaccination is *Caused* by the Vaccine

- ❑ **Most of the conditions that people worry about vaccines causing occur unrelated to vaccination**
 - Guillain-Barré syndrome occurs unrelated to immunization with about 1 case per year in 100,000 people
- ❑ **Except for the disease the vaccine prevents, all of the health outcomes – including deaths – that happen to people anyway keep happening after vaccination**

How Do We Decide if an Adverse Event is Caused by a Vaccine?

- ❑ Live virus vaccine strains can be isolated and distinguished by molecular techniques from “wild type” strains**
- ❑ Comparing the frequency that an adverse event occurs in a time interval after vaccination with the frequency that an adverse event occurs in a time interval that is not after vaccination**

How Do We Decide What We Are Going to Worry About?

- ❑ Consistent pattern of clinical findings**
- ❑ Biologic plausibility**
- ❑ Consistency of findings in other studies**
- ❑ Clustering of cases in time after vaccination, especially in a “biologically plausible” interval**
- ❑ Observed cases > expected cases**
 - Calculations require knowing what the incidence of the condition is, and how many doses of vaccine have been given

What Do We Do When We Find Something?

- ❑ **Communicate the finding to immunization providers and to the public**
- ❑ **Begin a field investigation or a research study**
 - Can the adverse event be prevented?
 - Who is at increased risk for the adverse event?
- ❑ **Reconsider risks and benefits of the vaccine**

Vaccine Safety: A Shared Responsibility

- ❑ **Immunization providers:** safe storage & handling, safe immunization practices, communicating risks and benefits, reporting of adverse events
- ❑ **Parents:** tell your doctor about allergies and previous adverse reactions, ask questions and get the information you need

What Immunization Providers Need to Know

UPDATE ON VACCINE SAFETY

Safety and Efficacy Issues Potentially Associated with the Childhood Vaccination Schedule

- ❑ Data generally available on concurrent administration at licensure**
- ❑ Interference between concurrently administered vaccines theoretically possible but generally not observed**
 - Need for spacing of live virus vaccines**
- ❑ Safety or efficacy issues associated with concurrent or antecedent exposure to vaccine components (e.g., diphtheria toxoid-containing vaccines)**
- ❑ Cumulative exposure to vaccine components**

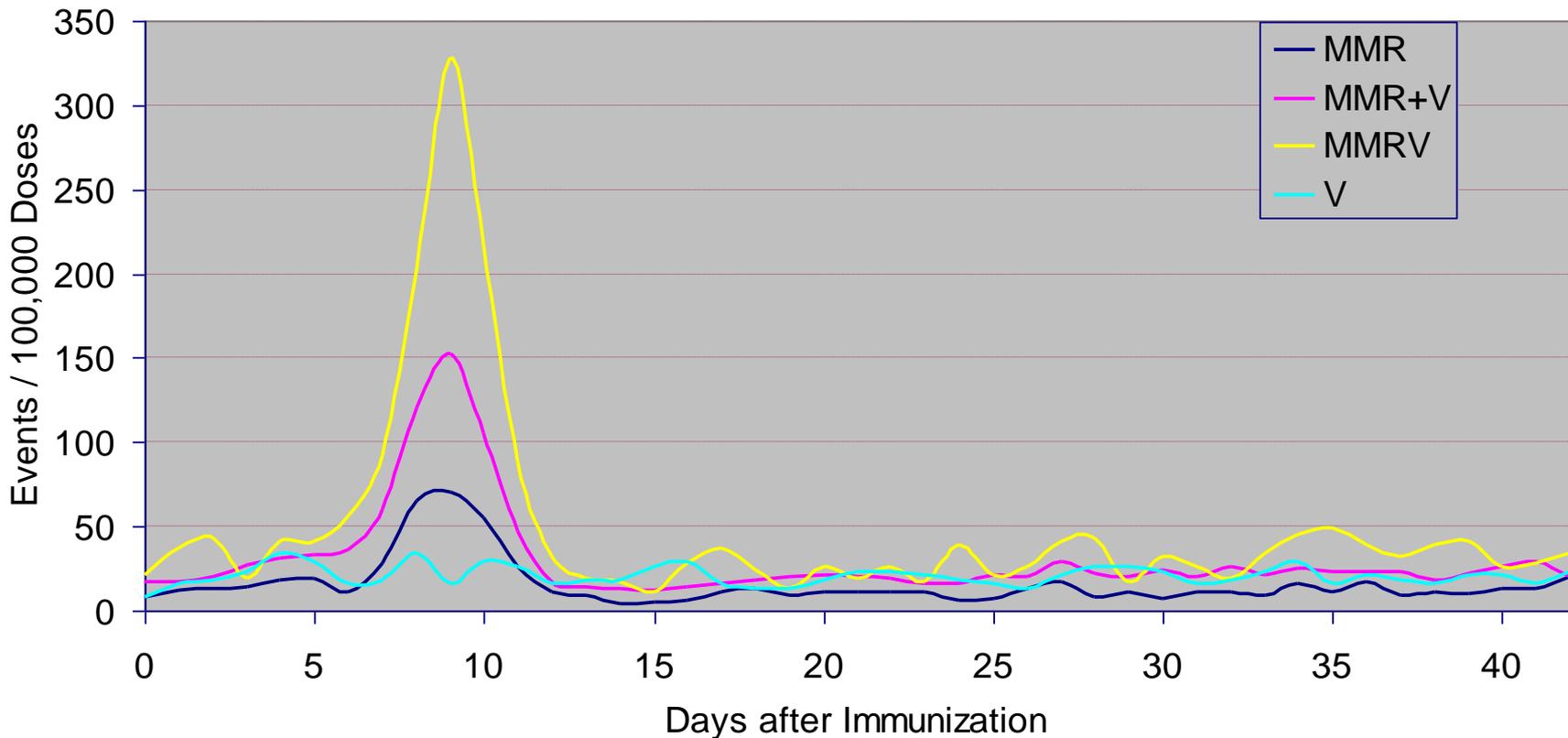
Data on Simultaneous Administration for a Licensed Vaccine: ROTARIX

- ❑ 484 healthy infants randomized into two groups**
- ❑ All received Pediarix, PCV7, and ActHib at 2, 4, and 6 months and either ROTARIX concurrently at 2 and 4 months or separately at 3 and 5 months**
 - Co-administration: n=249**
 - Separate administration: n=235**
- ❑ Prespecified criteria for noninferiority of antibody response met for all antigens**

Outpatient Visits for Fever by Day after Vaccine at Northern California Kaiser Permanente: 1995-2008

Age 12-23 months

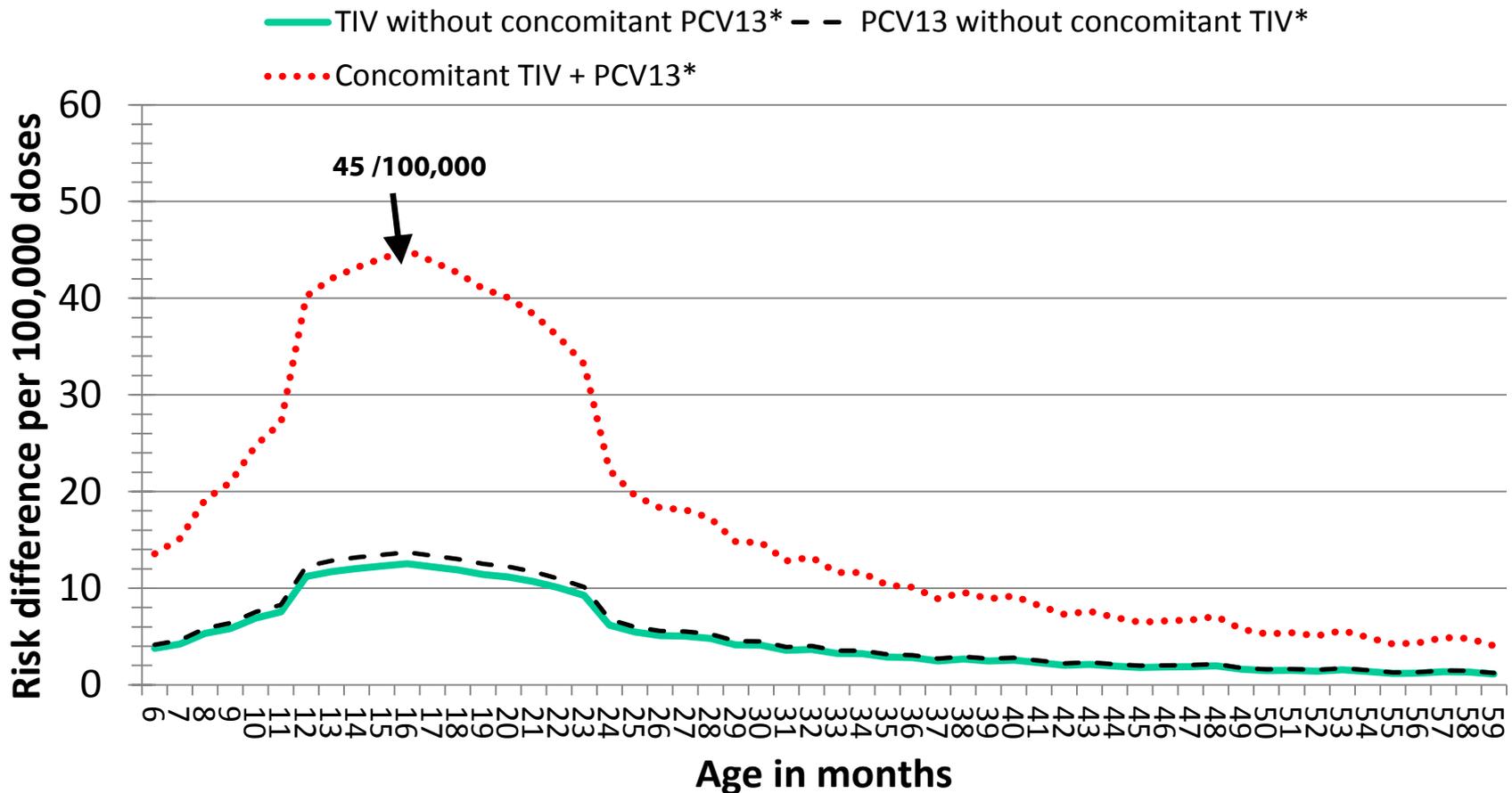
6241 total fever visits after 302,670 MMR+V, 147,762 MMR, 46,390 MMRV, 38,251 VZV



Febrile Seizures following MMRV

- ❑ In 2008 Rapid Cycle Analysis safety monitoring detected an increase in febrile seizures following MMRV
- ❑ MMRV was associated with a 2-fold increase in risk of fever and febrile seizures 7-10 days after MMRV compared with separately administered MMR+V among 12-23 month olds.
 - CDC recommended MMR+V unless parent/guardian prefers MMRV
- ❑ No increase in risk found for MMRV compared with MMR+V among 4-6 year olds.

Risk Difference (Excess Risk) Estimates for Febrile Seizures following 1st Dose TIV, 2010-11[†]



[†]Tse A and Lee G for the VSD

*Vaccines may have been received concomitantly with non-TIV, non-PCV13 vaccines

TIV, PCV13, and Febrile Seizures

- ❑ **Timely influenza and pneumococcal vaccination may prevent febrile seizures by protecting young children against influenza and pneumococcal infections, both of which can cause fever**
- ❑ **Clinical studies have not shown that fever-reducing medicines (e.g., acetaminophen, ibuprofen) prevent febrile seizures**
- ❑ **Aspirin and aspirin-containing products should not be used to reduce fever in children because of the increased risk for Reye syndrome with aspirin ingestion and viral infections**
- ❑ **Further investigation is underway to determine if other childhood vaccines besides TIV and PCV13 may be contributing to the febrile seizures**

Rotavirus Vaccines and Intussusception

- ❑ A very high risk (>30-fold) of intussusception in the first week following dose 1 of an earlier rotavirus vaccine led to its withdrawal in 1999
- ❑ Large prelicensure studies performed for both RotaTeq and Rotarix
- ❑ An elevated risk of intussusception following dose 1 found in postlicensure studies in Australia (RotaTeq) and Mexico (Rotarix) but not in Brazil (Rotarix)
- ❑ A postlicensure study of RotaTeq in the U.S. in the Vaccine Safety Datalink found no increase risk

Syncope (Fainting) following HPV Vaccine

- ❑ Increased reporting of syncope among vaccinees**
- ❑ Although usually not serious, syncope can result in falls, which sometimes cause serious injuries, especially head injuries**
- ❑ Syncope recognized to occur following vaccination, especially among adolescents and adults**

VAERS “Serious” Reports of Syncope following HPV Vaccine

- ❑ Total number of serious reports: 202**
- ❑ Injuries resulting from syncopal event:**
 - Fractures (nose, skull, maxillary)
 - Dental injuries
 - Contusions
 - Concussions
 - Intracranial hemorrhages (subdural hematoma, subarachnoid hemorrhage)
- ❑ No reports of death resulting from injury following a vasovagal syncopal event**

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

“... , although syncopal episodes are uncommon ... vaccine providers should strongly consider observing patients for 15 minutes after they are vaccinated. If syncope develops, patients should be observed until symptoms resolve.”

Verified VAERS Reports of Death following HPV Vaccine

- ❑ **Reported causes of death after clinical review with median onset interval:**
 - Neurological: 7 (Seizures 5, ALS 2); 53 days (13-745)
 - Cardiac: 7 (Arrhythmia 3, myocarditis 3, congenital); 9 days (2-25)
 - Pulmonary embolism: 4; 14.5 days (13-181)
 - Infectious: 5 (Group A strep 2, *N. meningitidis*, MRSA, HIV-CNS vasculitis); 29 days (4-117)
 - Other, noninfectious: 4 (suicide; type 1 DM DKA; drug overdose; dermatomyositis) 35 days (2-594)
 - Undetermined cause of death: 7; 17 days (2-121)
- ❑ **No patterns in verified death reports**

HPV4 Rapid Cycle Analysis Results: Vaccine Safety Datalink

- ❑ **VSD active surveillance confirmed no significant risk for any of the pre-specified adverse events after vaccination**
 - GBS, seizures, syncope, appendicitis, stroke, VTE, and other allergic reactions
 - Additional study is needed for a possible non-statistical association between HPV4 and VTE
 - All confirmed cases had other risk factors for VTE
- ❑ **No increase in rate of anaphylaxis following HPV4 as compared to previous VSD studies**

HPV Vaccine Safety: Summary

- ❑ **No new adverse event concerns or clinical patterns identified in VAERS review**
- ❑ **VSD rapid cycle analysis confirmed no significant risk for pre-specified adverse events* after vaccination for females 9-17years and 18-26 years**
 - GBS, seizures, syncope, appendicitis, stroke, venous thromboembolism (VTE), and other allergic reactions
 - Non-statistically significant increased relative risk of VTE among 9-17 year olds
- ❑ **Further evaluation of VTE post-vaccination ongoing**
- ❑ **Long-term follow-up of adolescents have not identified any safety concerns**

Wrong Drug Administered Mix-ups for 100 Random Reports

- **The most frequent vaccine combinations mix-ups from a random sample of wrong drug administered reports:**
 - Varicella-Zostavax mix-ups 25% (n=25) where:
 - Varicella given instead of Zostavax(16) Zostavax given instead of Varicella (9)
 - DTaP-Tdap mixups 11% (n=11)
 - DTaP given instead of Tdap (8) Tdap given instead of DTaP (3)
 - Pneumovax-Prevnar mix-ups 7% (n=7)
 - Pneumovax given instead of Prevnar(6), Prevnar given instead of Pneumovax (2)
- **10 (10%) reports also reported an adverse health event; two serious report (meningitis, otitis media/influenza).**
 - Adverse health events among non-serious reports: Injection site reaction (3) Fever (2) Respiratory (1), Constitutional symptoms (1), Allergic (1)

Eye Splashes and Rotavirus Vaccines

- ❑ **25 reports from 2006-2011* of an eye splash following administration of rotavirus vaccines.**
- ❑ **80% (20) reports involved an infant coughing, sneezing or spitting the vaccine into eyes.**
 - Eye splash by other means (4) and unknown exposure route (1).
- ❑ **Persons Affected by Eye Splash: 80% Health Care Providers, Patients 12% , Parents 8% .**
- ❑ **Adverse health event affecting the eye were reported in 64% (16) eye splash reports.**
 - All 16 reports that described an eye adverse event occurred in Health Care Providers and were non serious.

*Rotavirus vaccine was licensed in 2006. Error codes for accidental exposure and Grouped Eye MedDRA codes used in VAERS data analysis

Role of Clinicians in Preventing Vaccine Administration Errors

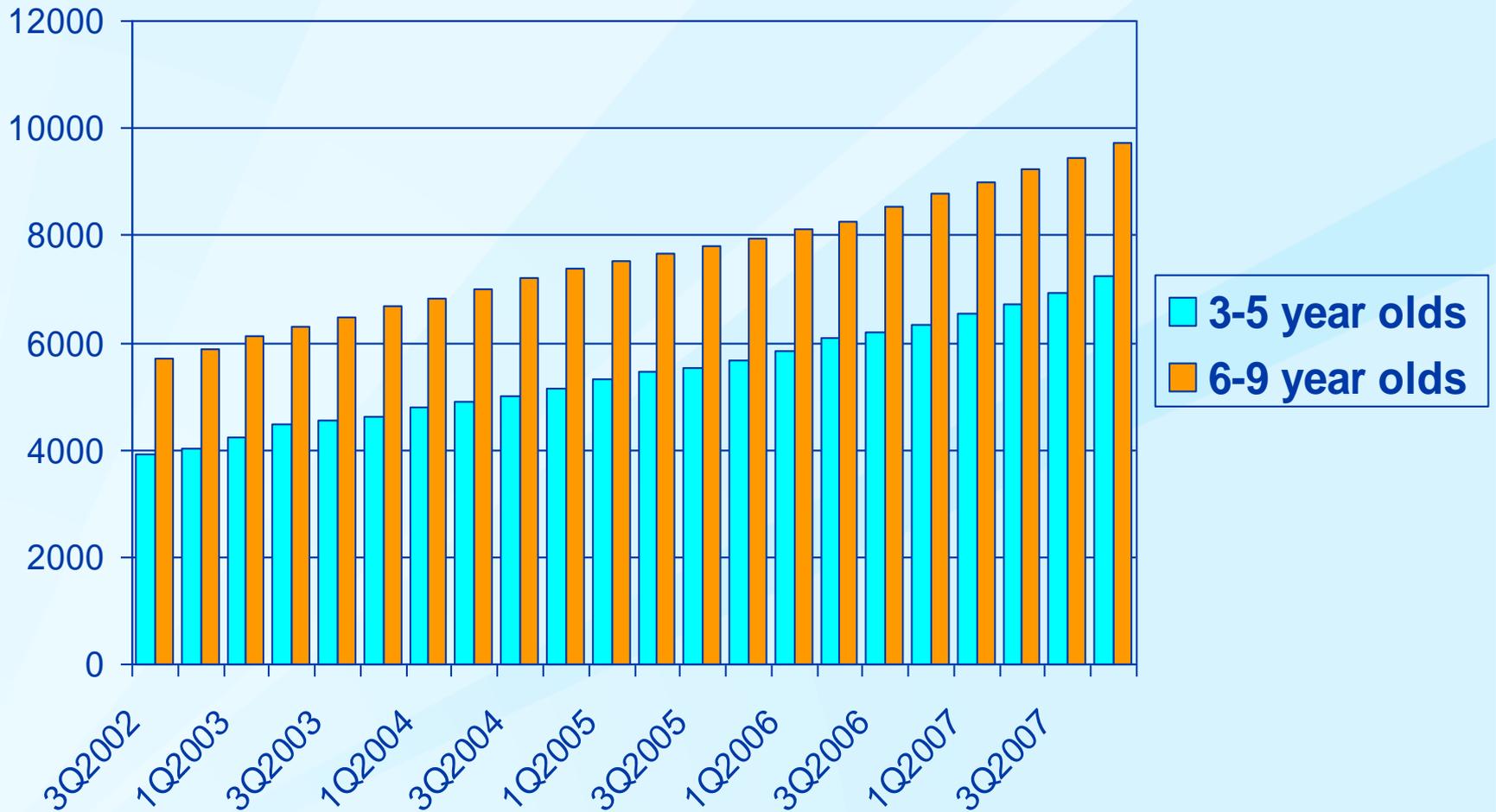
- ❑ **Proper Storage and Handling of Vaccines**
 - Vaccine Storage and Handling Guide (tool kit under revision), Pink Book Chapter 5, www.cdc.gov
 - <http://www.cdc.gov/vaccines/recs/storage/default.htm>
- ❑ **Identify Contraindications & Precautions**
 - Immunization Screening Questionnaires, www.cdc.gov
- ❑ **Proper Vaccine Administration -Right patient, Right time , Right dose, Right route, Right drug***
 - General Recommendations on Immunization www.cdc.gov
 - <http://www.cdc.gov/vaccines/recs/vac-admin/default.htm>
- ❑ **Report Clinically Significant Vaccination Errors to VAERS**
 - VAERS www.vaers.hhs.gov

*The five “rights” of medication administration

Thimerosal and Autism: What Does the Science Show?

- ❑ Ecologic studies: autism does not go down when thimerosal is removed from childhood vaccines**
- ❑ Epidemiologic studies: well-designed studies demonstrate no association between thimerosal exposure from vaccines and autism**
- ❑ Biochemical studies and animal models interesting but uninformative**

Children Receiving Autism Services by Quarter, California, 2002-2007



Vaccines and Autism, Still

- ❑ MMR and autism (1998)**
- ❑ Thimerosal and autism (2001)**
- ❑ Simultaneous administration of multiple vaccines and the “one size fits all” immunization schedule (2007)**
- ❑ Mitochondrial disorders (2008)**

Vaccines and Autism: Context

- ❑ **Heuristics and biases**
- ❑ **Distrust of government**
- ❑ **Unanswered questions about autism and real needs of families**
- ❑ **Advocacy**
- ❑ **Litigation**
- ❑ **Modern social networking tools**

“Why doesn’t CDC study autism rates in unvaccinated children?”

- ❑ Almost all children in the U.S. have received at least some vaccines; less than 1% of children have received no vaccines**
- ❑ Although recognized autism spectrum disorders more common than previously reported (up to 1 in 88 children), disease is infrequent enough that a large population needed to identify sufficient cases for a study**
- ❑ Unvaccinated children probably very different from other children in terms of:**
 - Healthcare utilization**
 - Other exposures**

Filling in Knowledge Gaps

- ❑ **Concerns about whole cell pertussis vaccine (DTP) and encephalopathy**
- ❑ **Dravet syndrome**
 - Severe disease with hard-to-control seizures, progressive course, poor prognosis
 - Many cases are associated with de novo mutations in a specific gene
- ❑ **A recent study suggests that many cases of encephalopathy after DTP are Dravet syndrome**

SMEI and “Vaccine Encephalopathy”

- ❑ **Epileptic encephalopathies, without other specific cause identified, with first seizure onset within 72 hours of vaccination**
- ❑ **Cases ascertained by child neurologists in Australia and New Zealand 2002-2003**
- ❑ **Diagnoses:**
 - SMEI – 8 patients
 - SMEB – 4 patients
 - Lennox-Gastaut syndrome – 2 patients
- ❑ **Molecular analysis:**
 - Heterozygous mutations of *SCN1A* in 11 of 14 cases

What Immunization Providers Need to Know

ADDRESSING PARENTAL CONCERNS

MACLEAN'S

**BARBARA AMIEL:
I'm home
alone P.12**

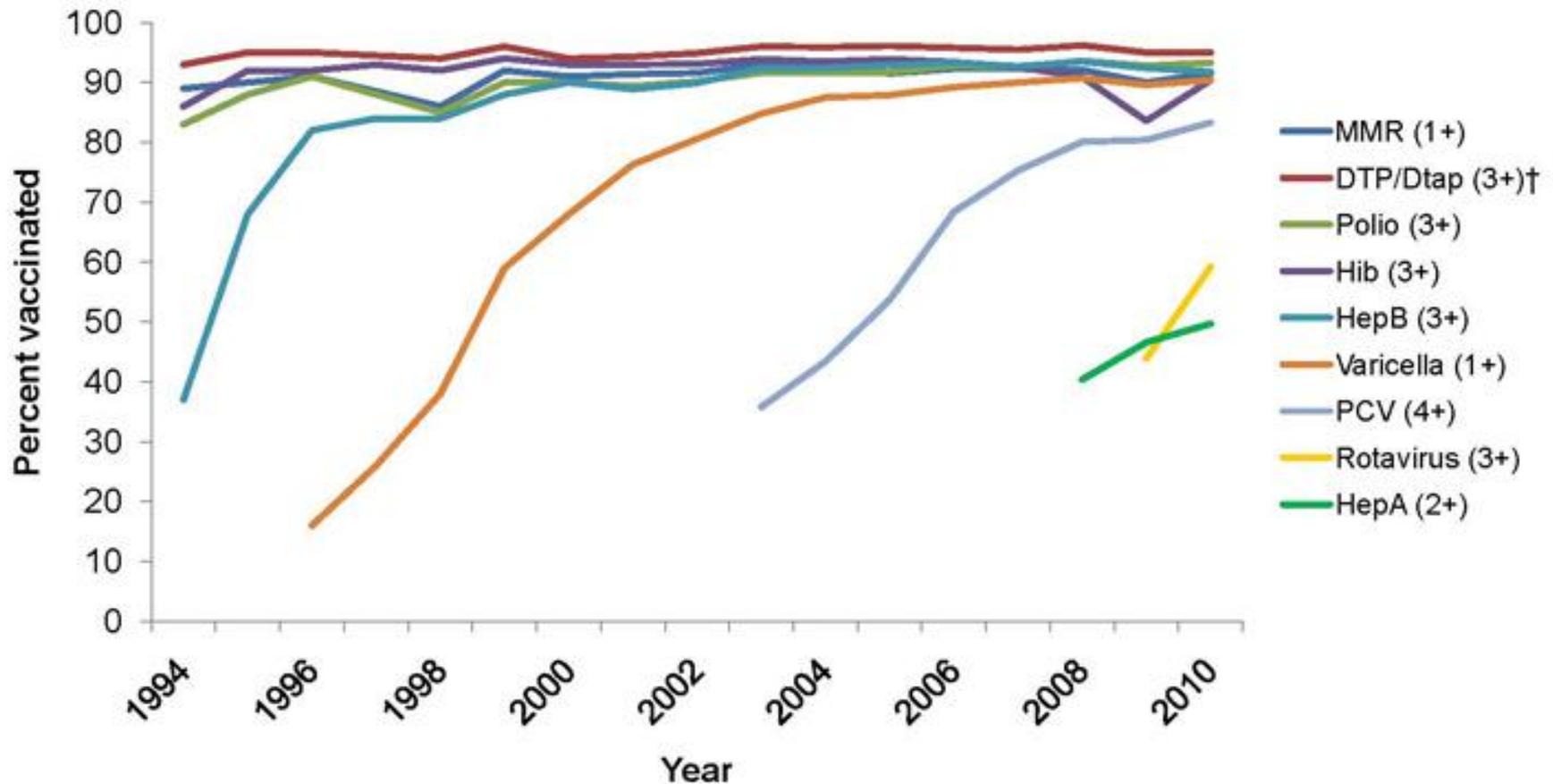
AUG.
27th
2017

OUR GIRLS AREN'T GUINEA PIGS

A mass inoculation of Canadian girls against a sexually transmitted virus is under way. Experts say it's unnecessary—and potentially dangerous.



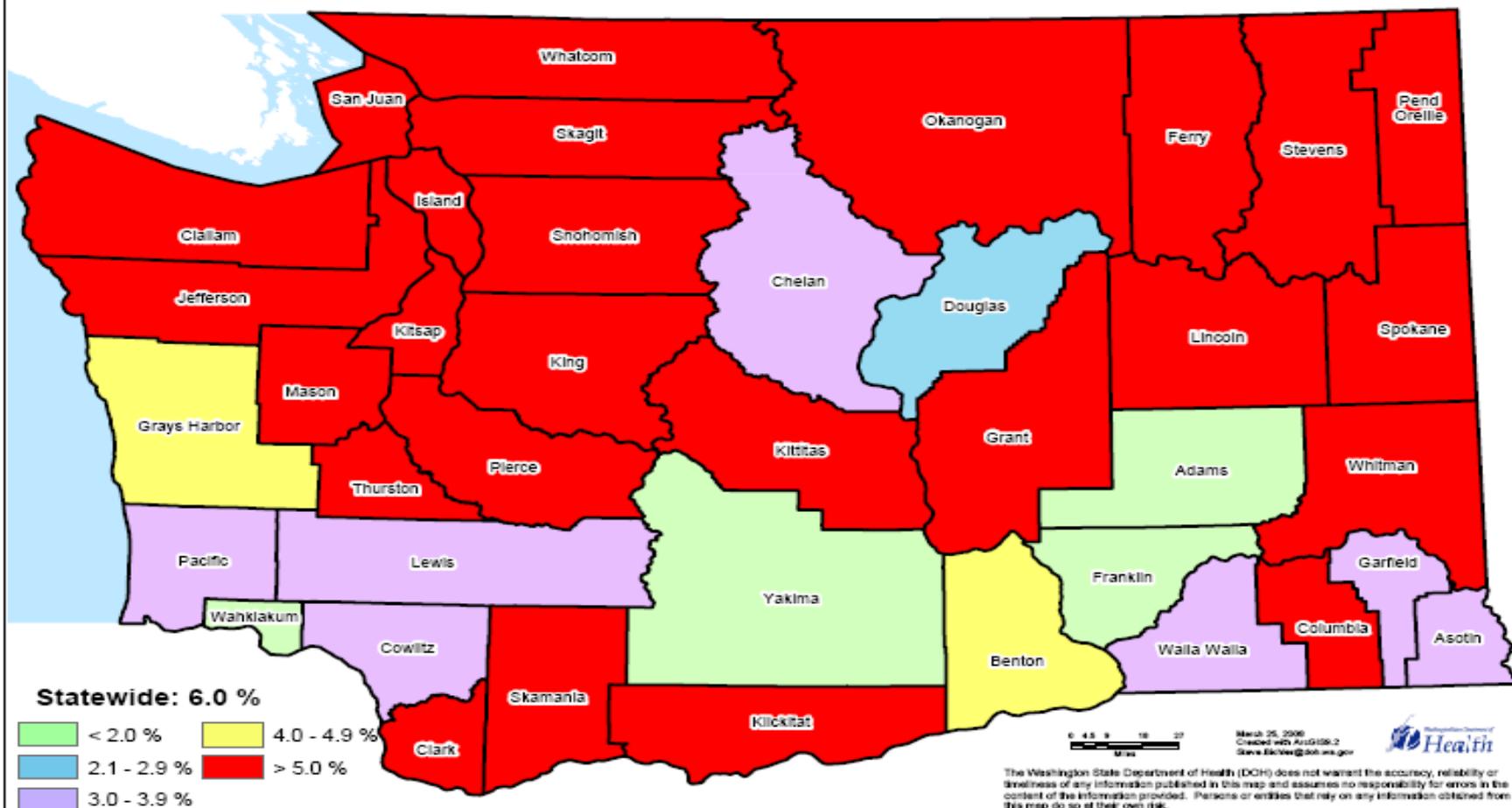
Vaccine-specific coverage* among children 19-35 months, National Immunization Survey, 1994-2010



* The Healthy People 2020 target for coverage is 90% for all vaccines with the exception of rotavirus (80%) and HepA (60%).

† DTP (3+) is not a Healthy People 2020 objective. DTaP (4+) is used to assess Healthy People 2020 objectives.

WA State Counties' School Entry Exemption Rates 2006-2007



Data source: Washington State DOH Immunization Program CHILD Profile

Invasive *H. influenzae* type B disease -- Minnesota, 2008

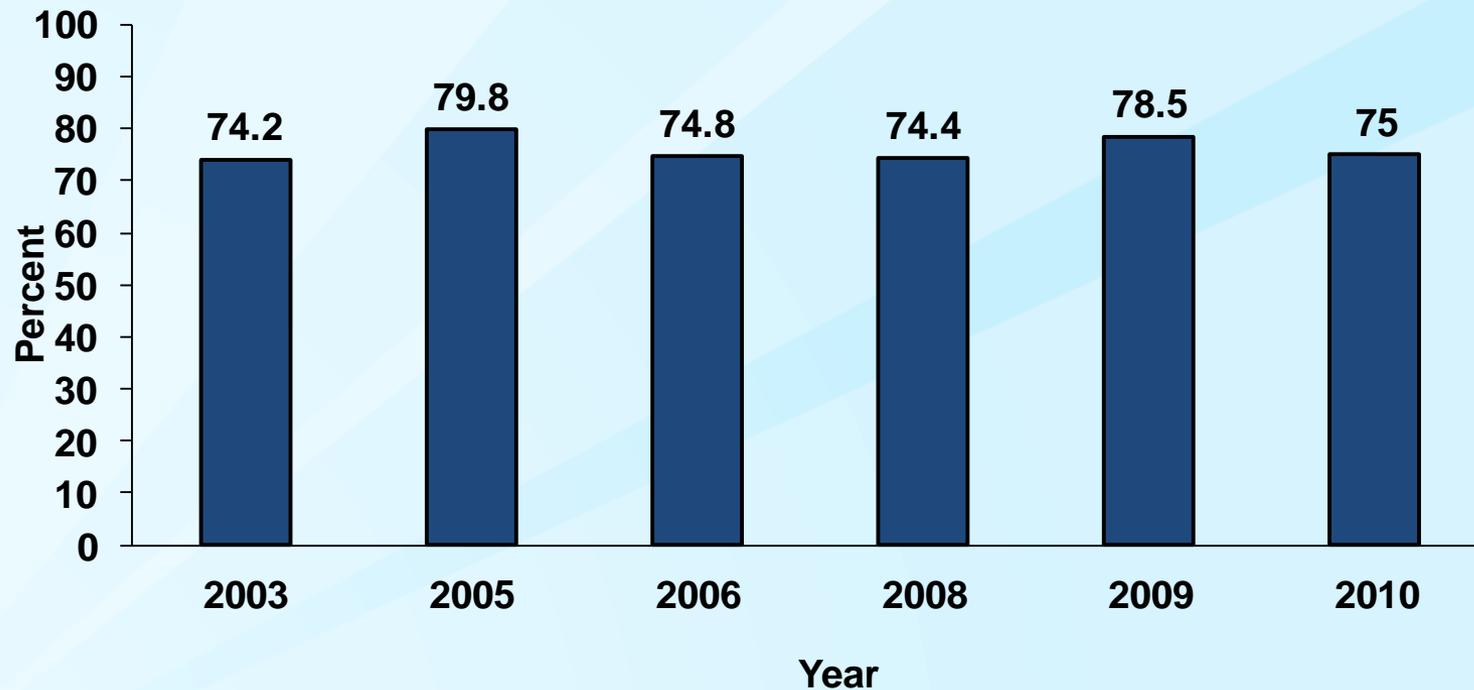
- ❑ 5 cases of invasive Hib disease in children <5 years of age; 1 death**
- ❑ Geographically dispersed and not epidemiologically linked**
- ❑ None of the children had been fully vaccinated against Hib**
 - 3 children had received no vaccinations because of parental refusal
 - 2 were partially vaccinated
- ❑ Occurred during national shortage of Hib vaccine that began in December 2007**

What Parents are Concerned About (2010)

- ❑ It is painful for children to receive so many shots during one doctor's visit (38%)**
- ❑ My child is getting too many vaccines in one doctor's visit (36%)**
- ❑ Children get too many vaccines during the first two years of life (34%)**
- ❑ Vaccines may cause learning disabilities, such as autism (30%)**
- ❑ The ingredients in vaccines are unsafe (26%)**
- ❑ Vaccines are not tested enough for safety (17%)**
- ❑ Vaccines may cause chronic disease (16%)**

Confidence in Vaccine Safety

Percent of parents who reported that they were confident or very confident in the safety of routine childhood vaccines



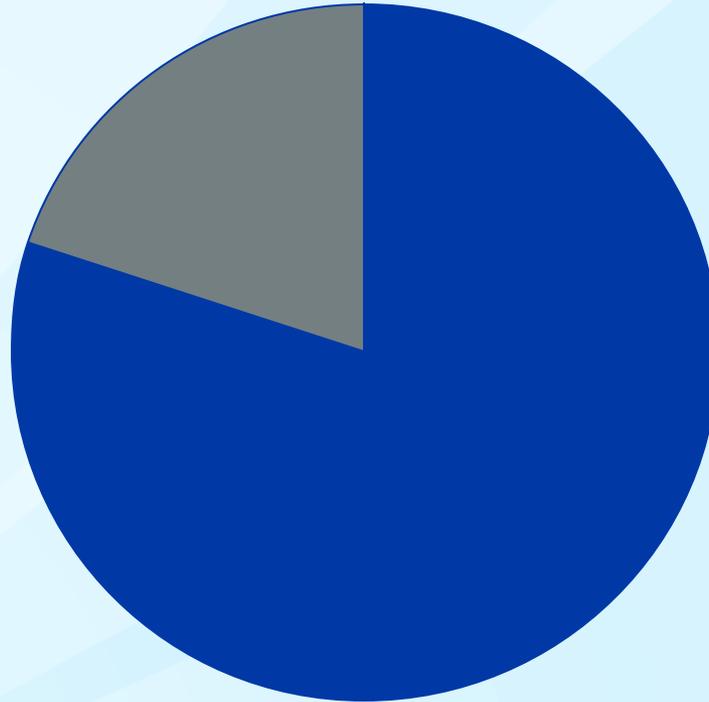
Source: PN Healthstyles

“What are the three most important sources of information that have helped you make decisions about your youngest child’s vaccinations?”

- ❑ Child’s health care provider (68.3%)**
- ❑ Family (45.4%)**
- ❑ Child’s other parent (22.7%)**
- ❑ American Academy of Pediatrics (21.8%)**
- ❑ Internet (17.5%)**
- ❑ CDC (17.0%)**
- ❑ Friends (14.8%)**
- ❑ Less commonly cited: traditional media, alternative health care provider, “other”, and “none of these”**

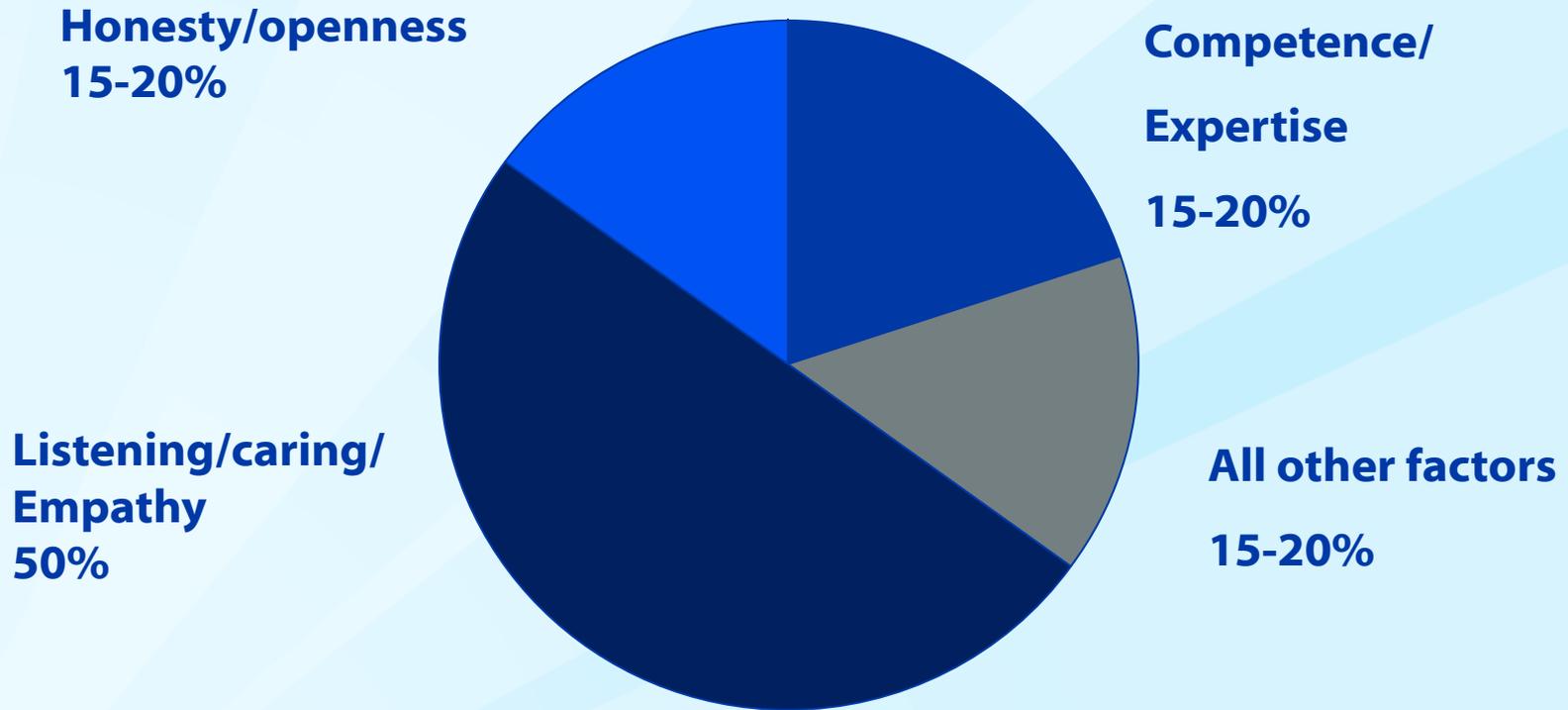
What Determines Credibility? Low Concern Settings

**All other
factors
15-20%**



**Competence/
Expertise
80-85%**

What Determines Credibility? High Concern Settings



Provider Resources for Vaccine Conversations with Parents

- ❑ Developed with partners: AAP and AAFP
- ❑ Primary target audience: healthcare professionals
 - Provide information to help when talking to parents about vaccines, vaccine-preventable diseases, and vaccine safety
 - Dual purpose: resources healthcare providers can provide to parents
- ❑ Based on formative, mixed methods research
- ❑ Using risk communication principles
- ❑ Extensively reviewed by subject matter experts

MEASLES

100 Degrees: A True Story

"You hear '100 degrees' you probably think that was 'not a baby's temperature. But for Megan Campbell, 30-month-old son, a fevering round of measles sent him to the hospital and caused fever spikes to 105 degrees."

"After picking up my son up at childcare because he had a fever," says Megan, "we went straight to our pediatrician who said our baby had a virus. No days later his fever hit 104 and a rash appeared on his neck."

"The rash quickly crept down to his arms and chest. San Diego-based Megan and husband Chris turned to the Internet. Finding pictures of measles that looked like their son's rash, they rushed him to the local clinic."

"No one there had seen it for about 17 years," says Megan. "I was expecting it in the year 2008 (as an infectious disease specialist)." "We spent three days in the ER. We might have our baby boy if we weren't so lucky. He seemed to be wasting away. I was able to drink again we got but the doctors told us to not to continue to try to breastfeed, which did make us feel a week, which it all hours to with fever reducing medication with damp wash cloths. I was worried because of signs nonresponsiveness. If we'd gone back to the hospital in Thanksgiving, the baby recover. Megan now knows that her son

DISEASES and the VACCINES that prevent them

Last updated: December 2008

Measles Symptoms

Measles begins with an increasing fever, then coughing, runny nose, or pink eyes, and finally a rash breaks out. The rash usually starts on the head and then spreads to the rest of the body. Fevers can persist, reaching extremely high temperatures, such as 104 for up to a week, and coughing can last about 10 days.

Measles Is Serious

According to Dr. Kathleen Gallagher of the Centers for Disease Control and Prevention (CDC), "Measles ranges from a pretty uncomfortable disease to a very serious one. For example, for every 1,000 children who get measles in a developed country like the U.S., one to three of them die, despite the best treatment. Even as recently as 2006 through 2007, one out of every four people in the U.S. who get measles had to be hospitalized." "Most of these serious cases

If You Choose Not to Vaccinate Your Child, Understand the Risks and Responsibilities.

Information for parents

If you choose to delay some vaccines or reject some vaccines entirely, there can be risks. Please follow these steps to protect your child, your family, and others.

With the decision to delay or reject vaccines comes an important responsibility that could save your child's life, or the life of someone else.

Information for providers

Talking with Parents about Vaccines for Infants

Physicians, nurses, and parents agree: times have changed. Because of questions or concerns about vaccines, well-child visits can be stressful for parents. As their infant's healthcare provider, you remain parents' most trusted source of information about vaccines, and your personal relationship uniquely qualifies you to help support parents in understanding and choosing vaccinations. However, time for infant health evaluation at each well visit is at a premium, as you check physical, cognitive, and other milestones and advise parents on what to expect in the coming months. Therefore, making time to talk about vaccines may be stressful for you. But when an infant is due to receive vaccines, nothing is more important than making the time to assess the parents' information needs as well as the role they desire to play in making decisions for their child's health, and then following up with communication that meets their needs. When it comes to communication, you may find that similar information—be it science or anecdote or some mix of the two—works for most parents you see. But keep a watchful eye to be sure that you are connecting with each parent to maintain trust and keep lines of communication open. We hope that these brief reminders—and the materials that you, your staff, and parents can find on our website—will help ensure your continued success in immunizing infants and children. Success may mean that all vaccines are accepted when you recommend them, or that some vaccines are scheduled for another day. If a parent refuses to vaccinate, success may simply mean keeping the door open for future discussions about choosing vaccination.

Before an outbreak of a vaccine-preventable disease occurs in your community:

- Talk to your child's doctor or nurse to be sure your child's medical record is up to date regarding vaccination status. Ask for a copy of the updated record.
- Inform your child's school, childcare facility, and other caregivers about your child's vaccination status.
- Be aware that your child can catch disease from people who don't have any symptoms. For example, EBV (mononucleosis) can be spread from people who have their bacteria in their body but are not ill. You can't tell who is contagious.

This resource owners:

- What you may hear from parents about their vaccine safety questions and how to effectively address them when raised
- Proven communication strategies and tips for having a successful vaccine conversation with parents

Nurses and other office staff can play a key role in establishing and maintaining a practice-wide commitment to communicating effectively about vaccines and maintaining high vaccination rates, then providing parents with educational materials, to being available to answer their questions, to making sure that families who may opt for other sites for vaccine receive and keep vaccine appointments.



U.S. Department of Health & Human Services
Centers for Disease Control and Prevention



AMERICAN ACADEMY OF FAMILY PHYSICIANS
STRONG BELIEVERS FOR AMERICA



American Academy of Pediatrics
MAKING IT THE HEALTH OF ALL CHILDREN

Talking with Parents about Vaccines for Infants

- ❑ **Healthcare providers are parents' most trusted source of information about vaccines**
- ❑ **Communication strategies**
 - Take time to listen and solicit questions
 - Acknowledge parents' feelings and emotions, including their desire to protect their children
 - Remind parents that you know their infant's health is their top priority, and it's yours too
 - Don't cut off the conversation
 - Be prepared to use both science and your personal experience
 - Acknowledge risks and benefits
 - Respect parents' authority
- ❑ **Reduce the stress of shots**
- ❑ **Document parents' questions and concerns**

It's Everyone's Job

Nurses, physician assistants, and other office staff play a key role in establishing and maintaining a practice-wide commitment to communicating effectively about vaccines and maintaining high vaccination rates.

From providing parents with educational materials, to being available to answer their questions, to making sure that families who may opt for extra visits for vaccines make and keep vaccine appointments, it's everyone's job.

www.cdc.gov/vaccines
www.cdc.gov/vaccines/conversations
www.cdc.gov/vaccinesafety

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

