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## ASSET Final Conference

Rome, October 30, 2017

### **Pandemic Influenza Preparedness Unsolved Scientific Questions**

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# Unsolved Scientific Questions

- **Efficacy of mandatory immunization**
- **Safety of the influenza vaccine in pregnant women**
- **Efficacy of influenza immunization in the elderly**
- **Efficacy of oseltamivir (Tamiflu)**





# Scientific Question 1

**Is Mandatory Immunization  
Effective?**

# Background

- **Vaccine hesitancy, including vaccine refusal, is becoming an increasing problem**
- **It has been responsible for a number of infectious disease outbreaks**
- **These include polio, measles and pertussis**



# Types of Vaccine Refusal

- **Ideological/Religious objections**
- **Fear of side-effects**
- **Lack of confidence in efficacy**
- **Lack of trust in selected vaccines**
- **Misinformation**



"This new mandatory STD vaccine shouldn't hurt a bit."

# Mom Jailed After Refusing to Vaccinate Her Child

[Melissa Chan/People](#) Oct 13, 2017

- A Michigan mother was jailed after refusing to vaccinate her 9-year-old son
- Rebecca Bredow was in contempt of court after she ignored an order from a judge that she had one week to get her son vaccinated
- Bredow: “Whether you are pro- or against vaccines, this is about the fact that my rights as a mother were taken away.”



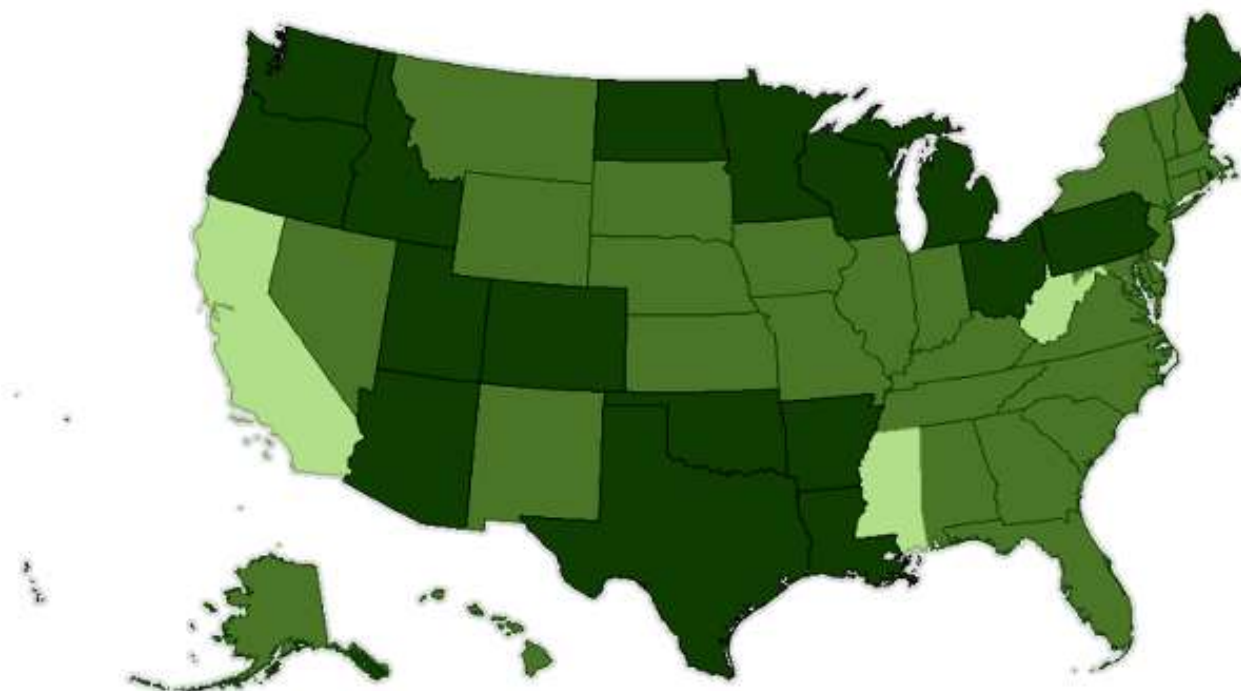
# Justification of Mandatory Vaccination

- **Vaccination is a way of preventing individuals from imposing unjust risk of harm on another**
- **However, compulsory vaccination requires authorities to balance public health with individual liberty**



# State Vaccination Exemptions: Medical, Religious, and Philosophical

(as of July 6, 2016)



■ medical ■ medical and religious ■ medical, religious, and philosophical



# Arguments against

- **May be unnecessary if vaccination rates are high even in countries that have not implemented strict requirements**
- **Puts additional cost and safety burdens on governments while perhaps reducing public trust and violating personal freedoms**



# Potential Problems

- **Mandatory vaccination laws may galvanize the anti-vaccination movement (joined by anti-vaccinationists and opponents to intrusion by governments on personal autonomy)**



# WHO and Individual Country Policies



- WHO has no official policy on mandatory vaccinations
- Some countries have mandatory vaccinations when faced with declining vaccination rates and outbreaks of disease



# Options for Enforcement of Vaccination

- Legal consequences include financial penalties, difficulty to attend public schools, or even penal consequences for the parents
- Enforcement varies in practice
- In some cases penalties are only theoretical and never applied



# Opinions of the US Courts

# Historical Cases in the US Courts

- *Jacobson v. Massachusetts* (1905), *Zucht v. King* (1922), and *Prince v. Massachusetts* (1944)
- Established precedents that personal and religious liberties cannot supersede the health of the children or the community
- Wei Zhu – <http://blogs.ssrc.org/tif/2015/05/22/5-questions-and-answers-about-religious-exemptions-for-vaccines/> Accessed 23-4-17

# Parental Refusal of Childhood Vaccines and Medical Neglect Laws

Parasidis E and Opel DJ. Am J Public Health. 2017;107:68-71.

- Searched court opinions from 1905 to 2016 and identified cases in which vaccine refusal was the sole or a primary reason in a neglect proceeding
- Most courts (7 of 9) considered vaccine refusal to constitute neglect





# *How will different countries in Europe respond to proposed legislation on mandatory vaccination?*

- **Countries in Europe will respond differently to a proposed legislation on mandatory vaccination**
- **Moreover, the distinct background and mentality of the people across Europe will definitely have an impact on the way they perceive this legislation.**
- **Also, the political dominance (conservative, liberal or other ideology) will influence the response**



# Scientific Question 3

**What is the Safety of the Influenza Vaccine in Pregnant Women?**

# The Study



## Association of spontaneous abortion (SAB) with receipt of inactivated influenza vaccine containing H1N1pdm09.

Donahue JG(1), et al. Vaccine. 2017;35:5314-5322.

- **Case-control study over two influenza seasons (2010-11, 2011-12)**
- **Cases had SAB and controls had live births or stillbirths and were matched on site, date of last menstrual period, and age**
- **The primary exposure window was the 1-28 days before the SAB**

# Results

- **Adjusted odds ratio (aOR) was 2.0 (95% CI, 1.1-3.6) for vaccination in the 28-day exposure window**
- **Among women who received vaccine in the previous influenza season, the aOR was 7.7 (95% CI 2.2-27.3)**
- **Based on 17 cases and 4 controls**
- **The aOR was 1.3 (95% CI 0.7-2.7) among women not vaccinated in the previous season.**

# Authors comments

- **Dr. Donahue - "There is no well-established biological mechanism to explain our observations.**
- **We do not fully understand all components of the immune response to the influenza vaccine and novel antigens (such as pH1N1), including the effects of repeated vaccination.**
- **Numerous studies have not shown a risk for miscarriage associated with influenza vaccination.**

# Conclusion

- **SAB was associated with influenza vaccination in the preceding 28 days among among women vaccinated in the previous influenza season with pH1N1-containing vaccine.**
- **This study does not and cannot establish a causal relationship between repeated influenza vaccination and SAB**
- **Further research is warranted.**

# The Media





# Devastating flu vaccine-miscarriage study sparks ridiculous spin

J.B. HANDLEY September 13, 2017

- *The mainstream media is doing their best to minimize a devastating study showing a high correlation (7.7-fold) between flu vaccines and miscarriages.*
- *A review of the scientific literature shows a body of evidence that supports the new study's conclusions.*



# Washington Post (Lena Sun)

- Researchers studying the flu vaccine in pregnancy have found a hint of a possible link between miscarriage early in pregnancy and the flu vaccine in women who received a certain version of the vaccine two years in a row

# Comments

- **JB Handley – “For those of you not steeped in the jargon of statistics or epidemiology, you’re going to have to take my word for it that “hint” is not a statistical term nor does “hint” in any way provide a specific assessment of risk”**
- **“Hint” is more like a word that you hope might keep people from reading your article**



## Scientific Question 2

# Efficacy of the Influenza Vaccine in the Elderly?

# Background

- **The current influenza vaccines are still not very immunogenic in the elderly**
- **Not clear whether an increase in dose or addition of adjuvants could provide a possible solution**



# Question

- **Will the double dose influenza vaccine reduce morbidity and mortality in the elderly, more effective than the standard dose?**





# Scientific Question 4

**How Sure Are We About the Efficacy of Tamiflu?**

# Findings

## CDC (Internet site)

- **RCTs among persons with mild illness in outpatient settings - zanamivir or oseltamivir can reduce duration of uncomplicated influenza A and B illness by about 1 day if given within 48 hours of illness onset**
- **Minimal or no benefit reported in healthy children and adults when initiated more than 2 days after onset of uncomplicated influenza.**



# Shedding of Virus

- **The amount of influenza viral shedding may be reduced among those treated**
- **Studies on the duration of viral shedding are inconsistent**
- **Temporal and causal relationships between changes in influenza viral shedding and clinical outcomes not well-established**

# Conclusion

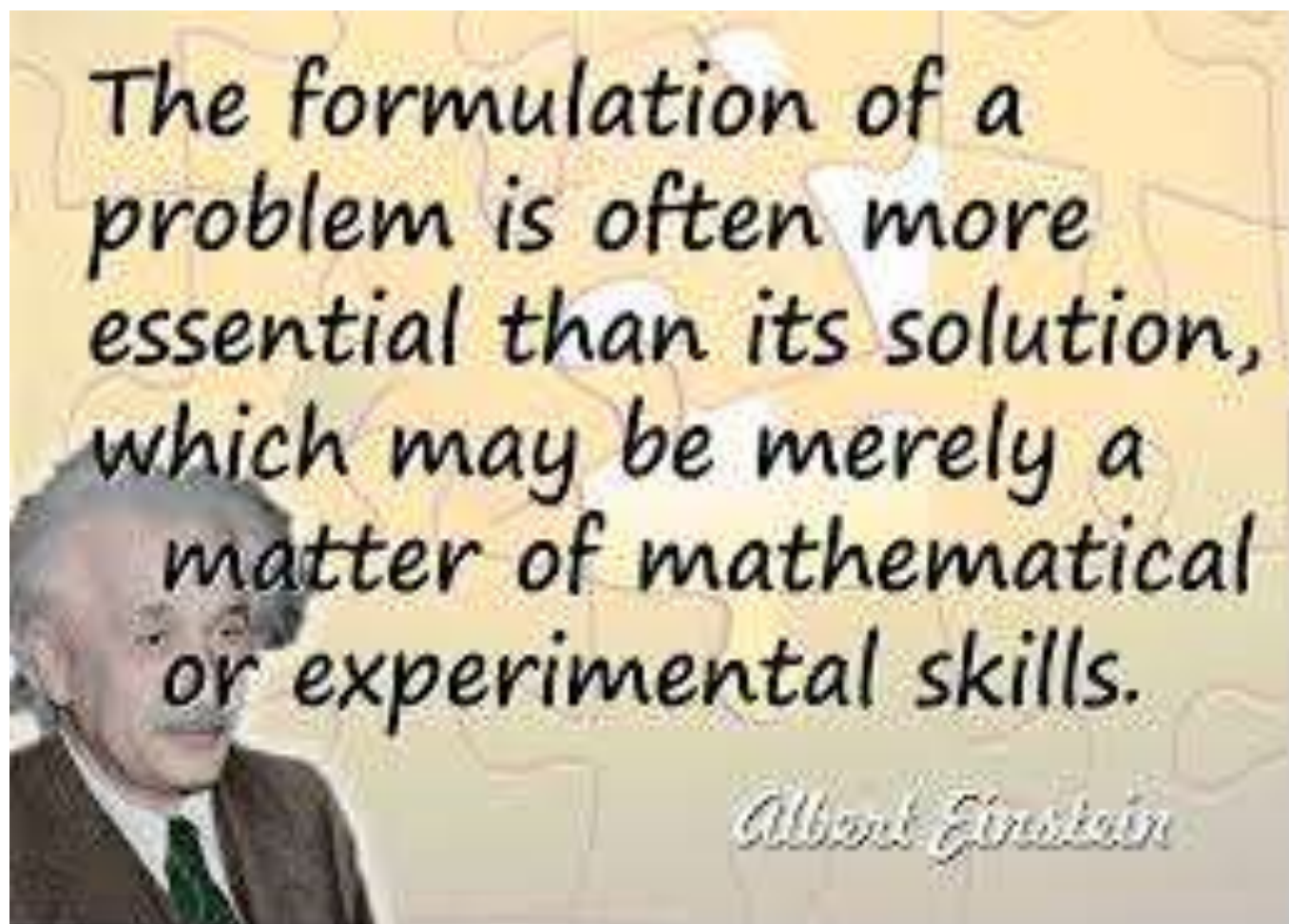


- **Not sure if wide-scale stockpiling of Tamiflu was justified**
- **Question of the influence of the pharmaceutical companies?**

# Summary

- **Numerous unsolved scientific questions in the control of influenza epidemics and pandemics**





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# Thanks for your attention!



A large, vibrant pink question mark with a white shadow, positioned centrally over a yellow rectangular background. The word "Questions" is written in a light blue, sans-serif font across the middle of the yellow background, with the question mark's stem passing through the letter 'e'.