

International Evaluation of the Risk of GBS following Pandemic Influenza Vaccine

An example of global collaboration

Presented by

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Background

- Vaccines are amongst the most effective public health interventions
- In many areas of the world, the very effectiveness of vaccines has eradicated public memory of the diseases they were designed to prevent.
- Safety scares have the potential to compromise or curtail vaccine safety programs both in the developing and developed world
- Safety scares now are globalizing in impact.

Common Threads in Recent Vaccine Safety Issues

- Often there is a lack of scientific evidence confirming a causative association with vaccine
- Because of the internet and effective global communication, scares which began locally have had a global impact.
- For rotavirus and intussusception, findings from the US stopped the vaccine in the developing world even though the risk-benefit may have been positive in many countries

Other Relevant Current Trends

- Vaccine development and manufacture of vaccines for export was once limited to Europe and the USA. This is no longer true with development of vaccines in Cuba, Brazil, India and China for actual or potential export
- Globalization of information exchange and of safety scares requires a coordinated response.
- Evaluation of rare events require large exposed populations... larger than may exist in one country alone.

Global Vaccine Safety Data Network

Prior History

- A meeting was held in Annecy in September 2007 to discuss the desirability and feasibility of a global vaccine safety data network.
- Participants included representatives from 22 countries including potential investigators, regulators, manufacturers, governmental and WHO, IVI, PATH, Sabin Institute, GAVI WHO representatives.
- The consensus of those attending was that establishing a global network of collaborating sites dedicated to the assessment of vaccine safety using clinical databases was both feasible and desirable.

Countries that Participated at the 2007 Meeting

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Capacity Survey Summary 2007

- Capacity and experience varied widely, but by country rather than by region.
- Countries with regional or national data on immunization, demographic and hospital outcomes:
 - Australia, New Zealand, China, Singapore, Brazil, Costa Rica, Canada, USA, Denmark, Italy, UK, Mexico, Vietnam, Thailand, Belgium
 - Potential population > 75 million people
- Countries with hospital outcomes data without immunization registries:
 - Switzerland, South Africa, Chile, Germany, Finland
- Data systems and localization (national, regional) are variable.
- Several countries had experience using computerized data for vaccine safety analyses:
 - New Zealand, USA, Denmark, UK.

International Study on GBS and Panemic H1N1: A Proof-of-concept

- Immediate objectives:
 - To pilot an international collaborative approach towards the implementation of a simple and reliable epidemiological study methodology
 - To investigate the association between GBS and H1N1 pandemic vaccines
- Final Goal:
 - To validate that this collaborative approach should be generalizable to other countries
 - To justify the establishment of sustainable infrastructure for a global collaboration which would include developed, middle income and low income countries.

Current International Study on GBS and H1N1 pandemic vaccines : Background

- Multiple H1N1 influenza vaccines developed/distributed worldwide for pandemic use
- H1N1 vaccines used extensively in population groups not often vaccinated against influenza
- Limited capacity for epidemiological vaccine safety studies in many countries
 - Often rely on passive surveillance for post-marketing safety
- H1N1 vaccine safety concerns provided opportunity to demonstrate feasibility of a global collaborative vaccine safety consortium

Why GBS?

- GBS was associated with the 1976 Swine Flu vaccine and is of concerns for most countries.
- The Brighton collaboration had developed a widely accepted case definition which can be used to standardize assessment
- In most countries GBS cases are hospitalized and thus can be ascertained in an unbiased manner from hospital records.
- GBS is a rare outcome, few countries have sufficient population to perform a valid study on their own

What Data is Needed for a Data Network?

vaccine
Data

**Exposure information
at a minimum for cases**

Computerized Hospital
And/or Clinic Diagnoses

**Outcome or Possible
“Adverse Event”**

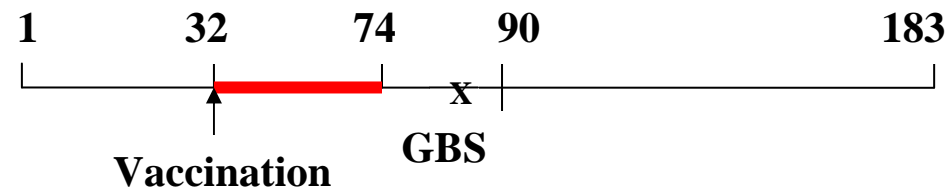
Demographic Data on
A Population

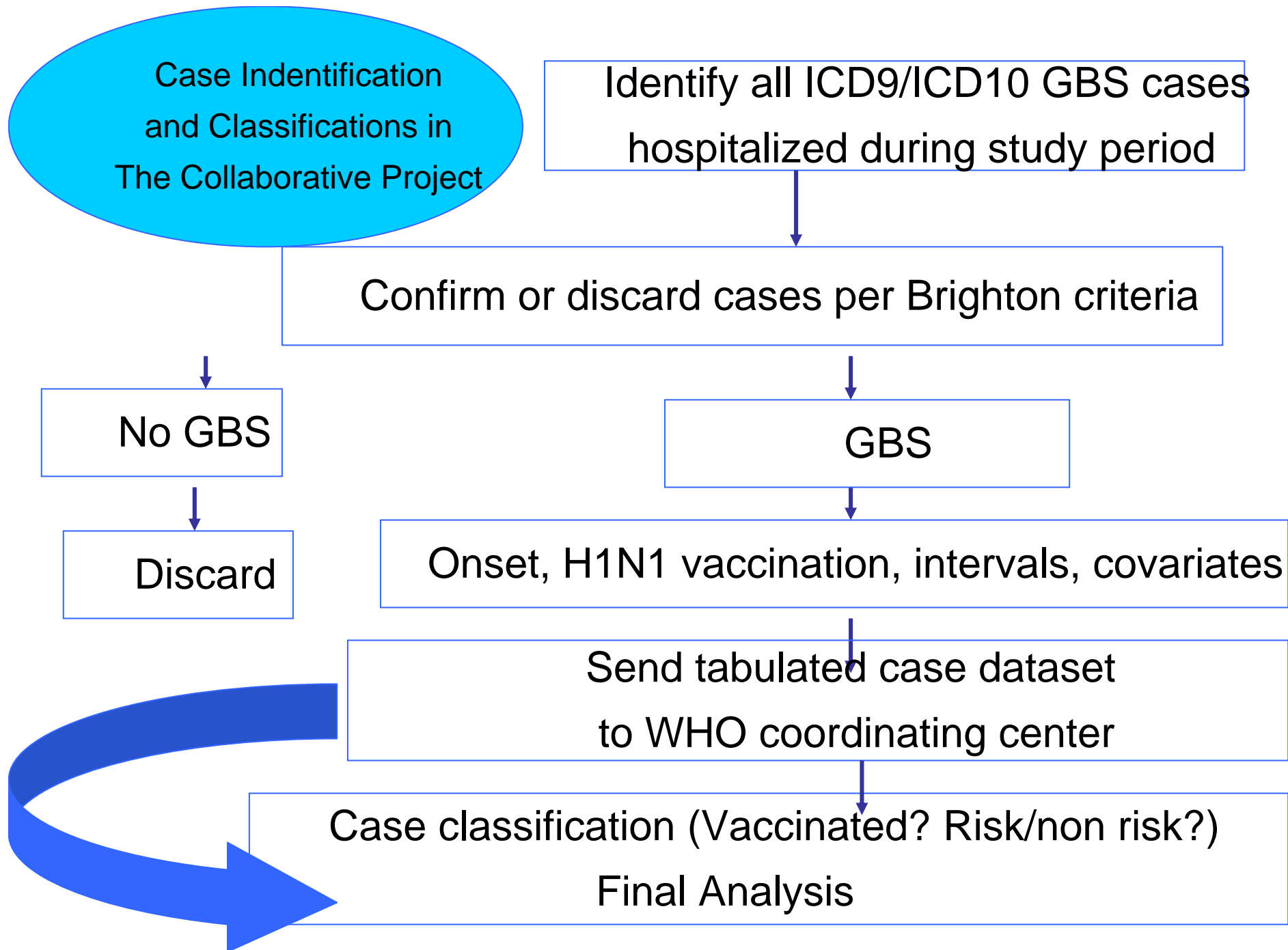
NOTE:

- Can do case series with Outcome alone or case control with Outcome and Demographics.
- With all three, can calculate rates and attributable risk

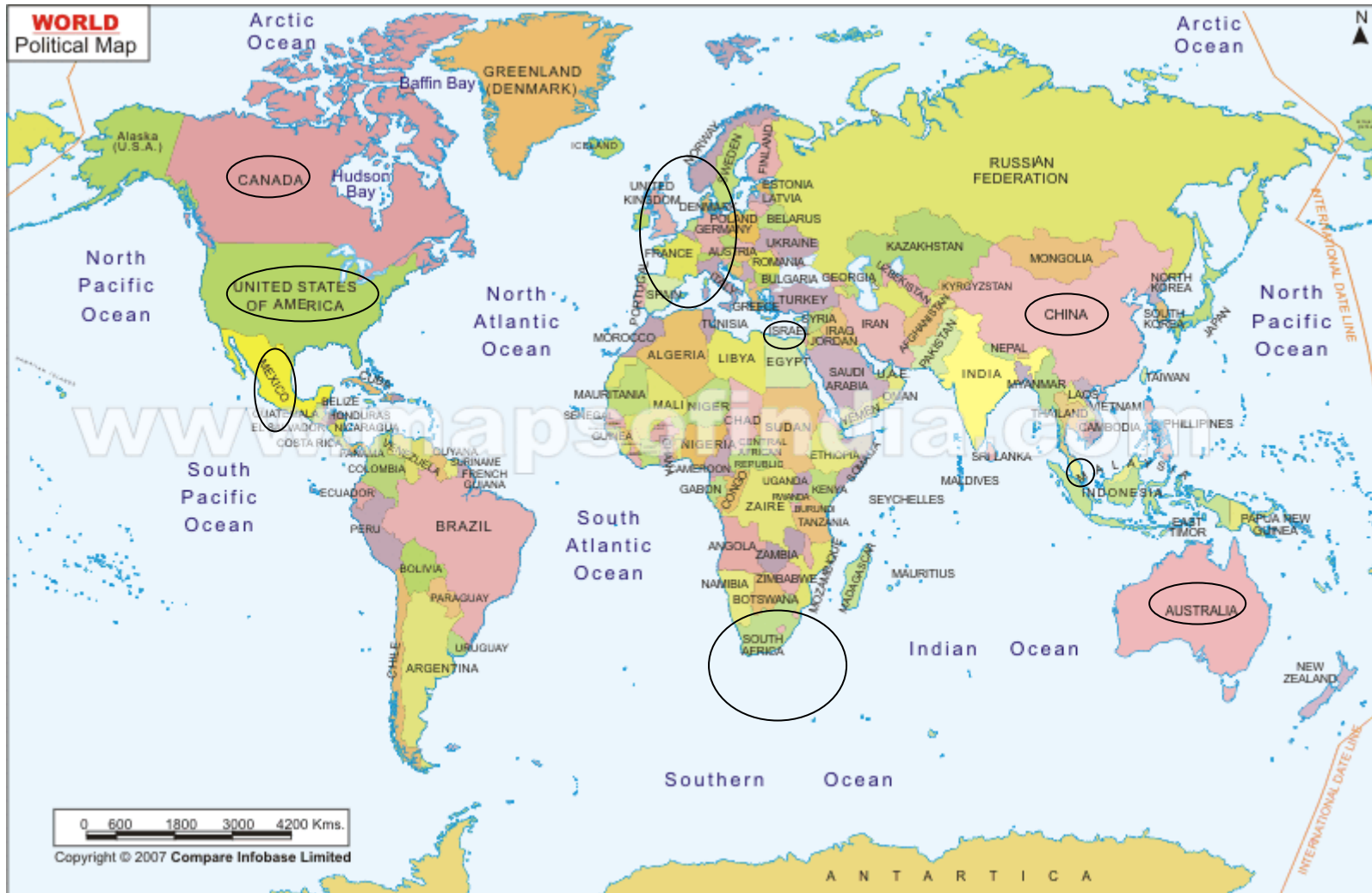
Standard SCCS Method

- Example, individual i , observation period: 10/15/09-4/15/10 (day 1 to 183),
vaccination: 11/15/09(day 32), risk window:
day 1-42, season cut off: 1/12/09 (day 90),
diagnosis: 1/5/10 (day 83)





Participating Countries



Current Status: Country Data

Country	Site/System	GBS Case *		
		Total	Received H1N1	Received seasonal flu
Australia	Adelaide	1	0	0
	Sydney	5	1	0
Canada	Quebec	pending		
China	Hong Kong	24	6	9
	Shanghai	29	0	0
Israel	Maccabi	12	1	1
Mexico				
Singapore	Singapore	19	4	1
Spain	Barcelona	14	0	2
	Valencia	10	0	2
	Almeria	8	1	0
USA	CMS	pending		
	DoD, VA			
	PRISM			
	VSD	13	13	11
VAESCO	EU	pending		
Total		135	26	26

Cases reported to WHO as of January 2011.

Benefits of a Global Vaccine Safety Data Network

- An unsubstantiated vaccine safety scare could incapacitate a valuable vaccine program.
- Without a ready infrastructure, responding to such a scare or safety issue could take so long that the program could be dead by the time an analysis is done.
- Lack participation of local experts can undermine credibility of results
- Allows evaluations of safety concerns across a large population
- Allows retesting of results from one country in another setting
- Provides a basis for mentoring and facilitating development of infrastructure where it currently does not exist.
- Supports evidence-based decision making by the WHO GACVS and other bodies.

Importance of Broad Based Participation

- With globalization of vaccine manufacturing, globalization of evaluation is required.
- Increasing focus on development of vaccine targeting the developing world requires safety evaluation infrastructure in the same geographic area.
- Potential variability in susceptibility to adverse events requires a diverse population to evaluate vaccine safety

Summary of Current Status

- Need has been demonstrated and is generally accepted
- Feasibility of within country and intracountry collaborative studies has been demonstrated
 - VAESCO
 - Global Vaccine Safety Collaborative Network:
 - Pilot project to assess risk of GBS following H1N1 pandemic influenza vaccine
- However, the global network is only a demonstration project and would require resources to become sustainable.

What is needed to go forward?

- Sufficient infrastructure to supervise activities, prioritize projects, provide analytic capacity and coordination
- Ability to assess data quality across sites
- Ability to mentor new sites
- A sustainable source of resources: Two models which are not mutually exclusive
 - A central foundation which receives funds from donors, from a vaccine excise tax or similar source.
 - A central foundation which receives support for selected projects from manufacturers with specific need to perform phase four studies.
- Conclusions
 - We have moved forward in the past four years, but progress has been slow.
 - Unless a reliable source of support is identified and sustainable infrastructure established, international collaborations run a high risk of being unsustainable.