



Influenza Vaccine Use In the Americas
Network for Evaluation of Influenza Vaccine Effectiveness
REVELAC-i

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Outline

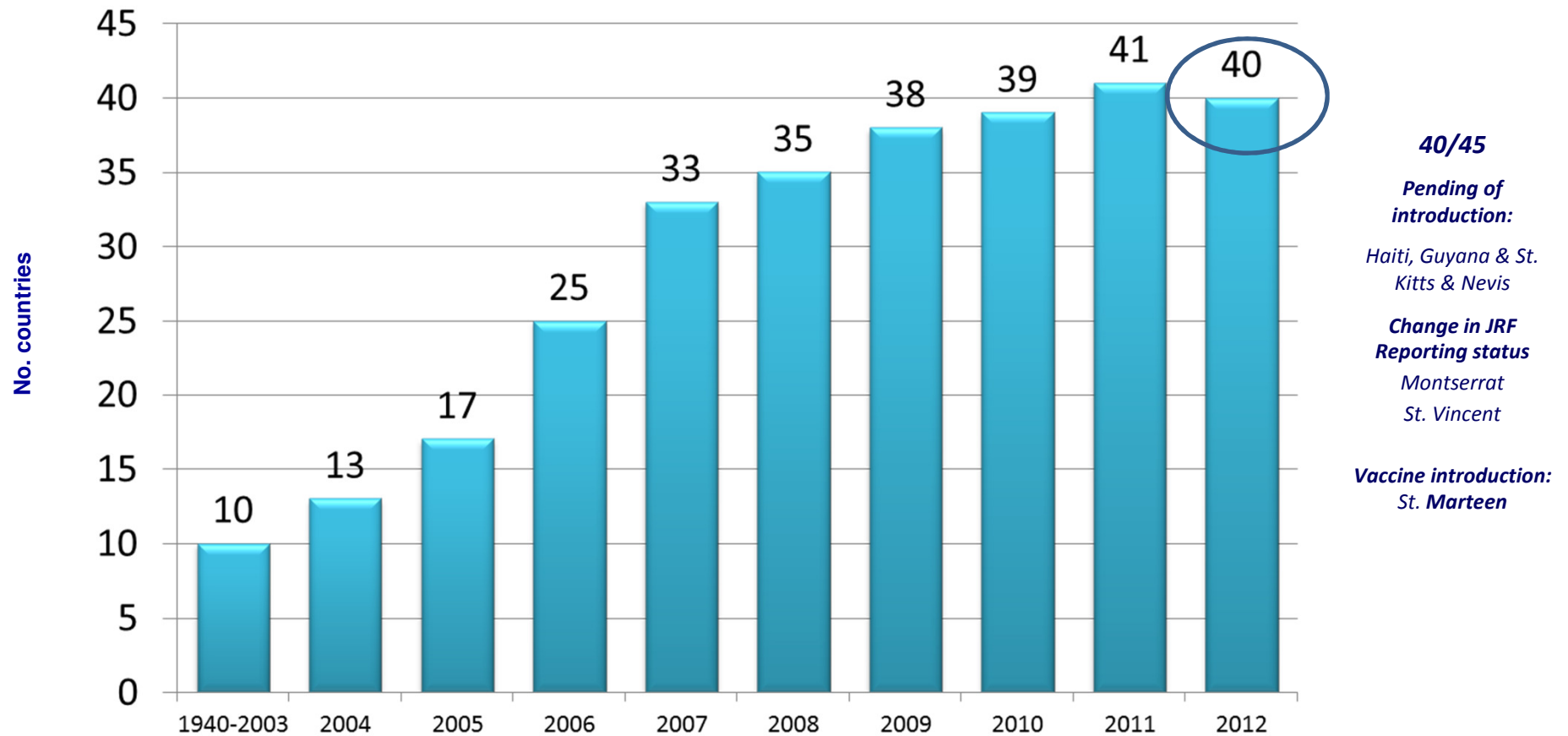
- I. Uptake of Seasonal Influenza Vaccination in LAC**
- II. Background REVELAC-i**
- III. Challenges of using current data for vaccine effectiveness evaluation and how nominal registries can help**

Criteria for influenza vaccine introduction in Latin America and the Caribbean

Countries and territories in the Americas identified several criteria used to justify seasonal influenza vaccine introduction:

- PAHO's TAG, WHO and ACIP recommendations
- Burden of disease
- Political decision-making
- Cost-effectiveness studies
- As part of the preparation for H5N1 influenza pandemic

Countries and Territories in the Americas with Policies for Seasonal Influenza Vaccination, 2003-2012



Source: Country Reports to PAHO, MOH web pages, PAHO/WHO Surveys

Note: Data was not collected from the French Departments (French Guiana, Guadeloupe, Martinique)

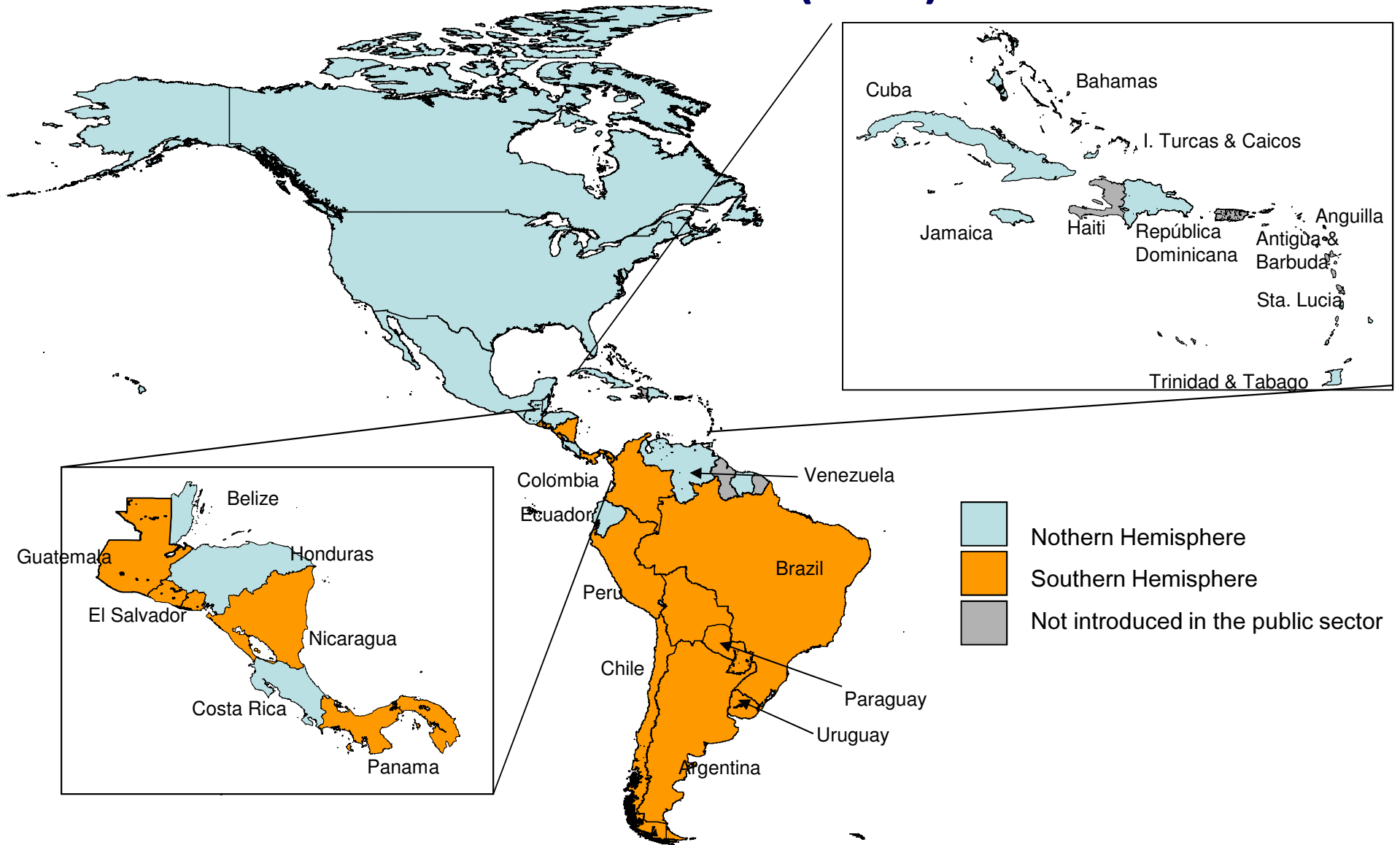
Countries and territories in the Americas with policies for seasonal influenza vaccination

| Number of countries with: | 2004 | 2008 | 2012 |
|--|------|-------|------|
| - Vaccination of healthy children | 6 | - 22 | - 25 |
| - Vaccination of only children with chronic diseases | --- | - --- | - 10 |
| - Vaccination of elderly | 12 | 33 | 38 |
| - Vaccination of persons with chronic diseases | 9 | 24 | 32 |
| - Vaccination of health workers | 3 | 32 | 37 |
| - Vaccination of pregnant women | 3 | 7 | 22 |

Source: Country Reports to PAHO, MOH web pages, PAHO/WHO Surveys

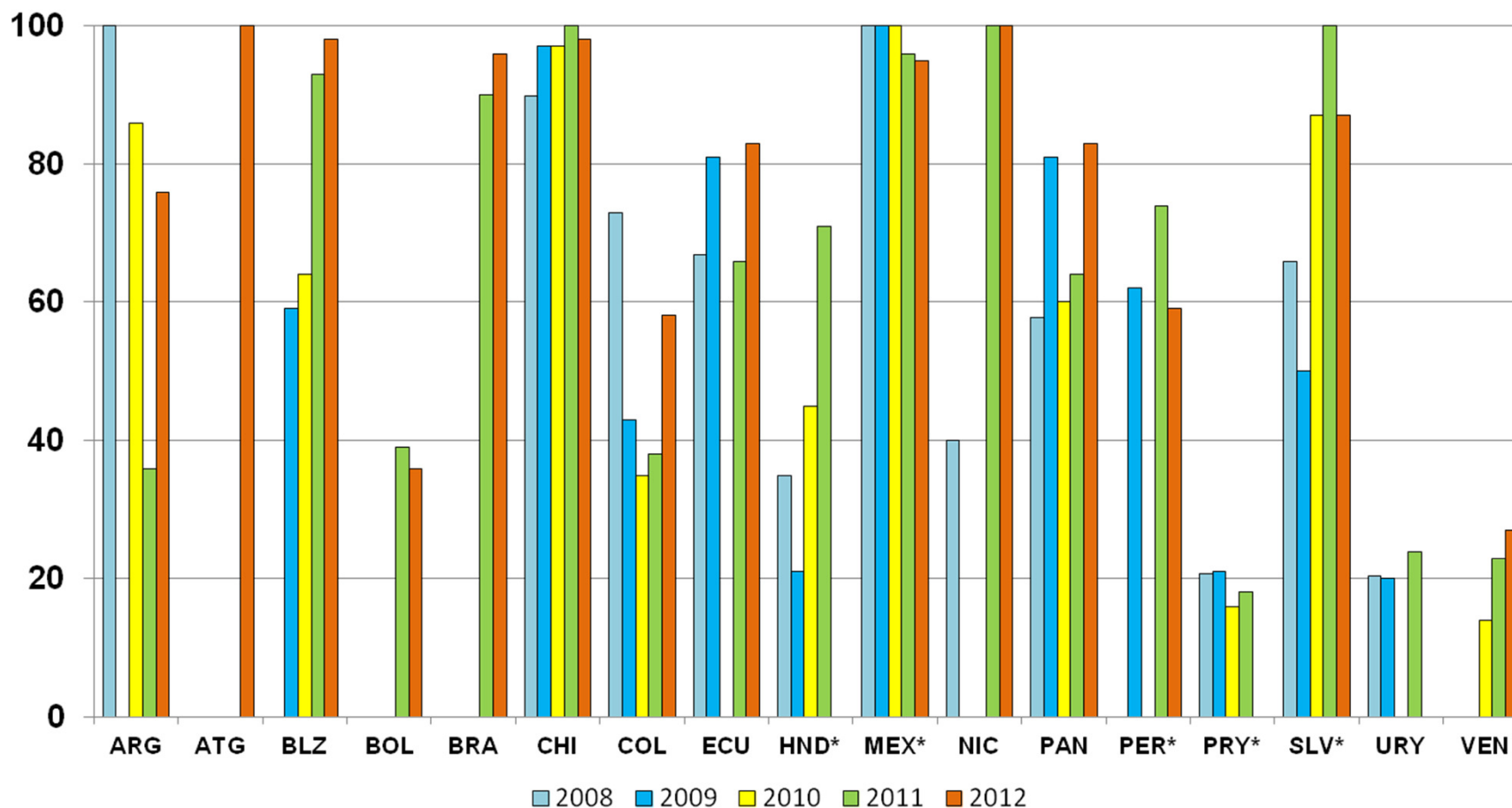
Note: Data was not collected from the French Departments (French Guiana, Guadeloupe, Martinique)

Use of Seasonal Influenza vaccine and formulation in the Americas (2012)



Source: Country reports to PAHO, MOHs Webpage, PAHO/WHO Surveys

Seasonal influenza coverage in children 6-23 months of age* in reporting countries, LAC, 2008-2012

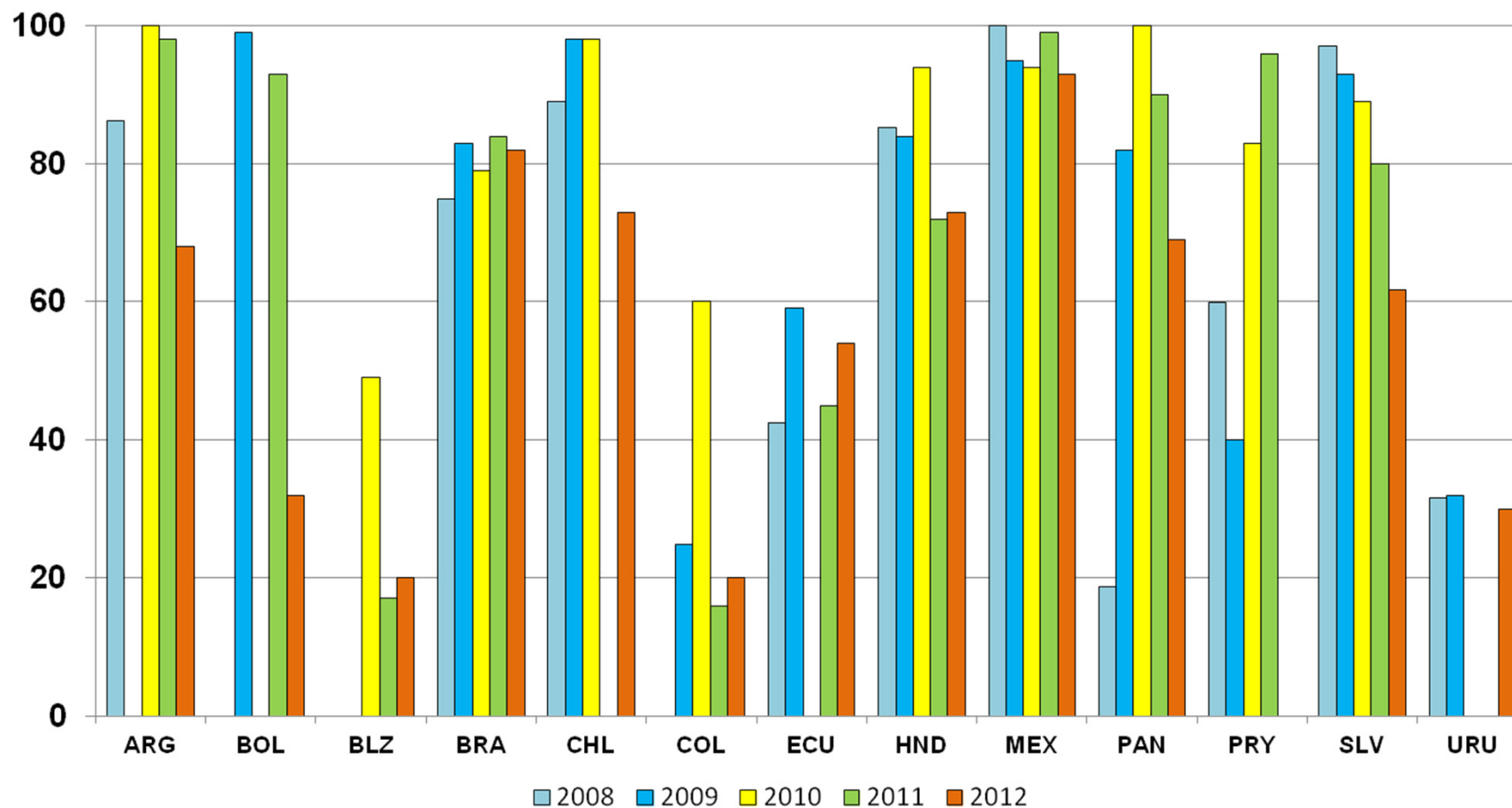


Source: Country reports to PAHO

* El Salvador in 2012, administered to children 6-59m; Honduras and Mexico administered to children 6m-35m;

Peru administered to children from 7m; Paraguay from 2008-2009 administered to children 6-23m and from 2010-2011 administered to children 6-35m

Seasonal influenza vaccination coverage among elderly in reporting countries, LAC, 2008-2012



Source: Country and territory reports to PAHO

Justification for conducting systematic vaccine effectiveness evaluations

- As influenza vaccines are reformulated every year to match the circulating viruses, (VE estimates from previous years cannot be used in the subsequent years)
- Monitoring VE can help guide the use of other complementary public health measures especially when the VE is low in any given year(antivirals, hand washing)
- Epidemiologic variability
 - ◇ Host factors (age, underlying conditions)
 - ◇ Different products (TIV/LAIV, adjuvanted/unadjuvanted)
 - ◇ Waning immunity over time.
 - ◇ Different settings, operational aspects of EPI vaccine delivery

Multicenter Evaluation of Influenza Vaccine Effectiveness in Latin America* - REVELAC-i

2012 Pilot phase

| Country | Target groups | |
|-------------|---|-----------|
| | Children | Elderly |
| Costa Rica | 6 months – 10 years with chronic diseases | ≥65 years |
| El Salvador | 6–59 months | ≥60 years |
| Honduras | 6–35 months with chronic diseases | ≥60 years |
| Panamá | 6–59 months | ≥60 years |

CDC, Influenza Division
 CDC-CAR, Influenza Program
 Pan American Health Organization

Protocol piloted in 18 sites

2013 Implementation



Red para evaluación de la efectividad de la vacuna en LAC -
 Influenza

| | |
|-------------|-----------|
| Argentina | Honduras |
| Brazil | México |
| Chile | Panamá |
| Colombia | Paraguay |
| Costa Rica | Uruguay |
| Cuba | Nicaragua |
| El Salvador | |

*Case-control (test-negative design) based on hospital sentinel SARI surveillance

Current progress

74 sentinel hospitals reporting SARI :

| Country | Target group | | N hosp |
|--------------------|---|-----------|--------|
| | Children | Elderly | |
| Argentina | 6–24 months | ≥65 years | 4 |
| Brasil | 6–23 months | ≥60 years | 29 |
| Chile | 6–23 months | ≥65 years | 6 |
| Colombia | 6–23 months | ≥60 years | 7 |
| Costa Rica | 6 months–10 years with chronic diseases | ≥65 years | 6 |
| Cuba | 6–23 months | ≥65 years | TBD |
| El Salvador | 6–59 months | ≥60 years | 4 |
| Honduras | 6–35 months with chronic diseases | ≥60 years | 3 |
| México | 6–59 months; 3–9 years with chronic diseases. | ≥65 years | TBD |
| Panamá | 6–59 months | ≥60 years | 10 |
| Paraguay | 6–35 months | ≥60 years | 2 |

Countries and networks reporting vaccine effectiveness annually

| Study | Setting | Study population | Case definition | Vaccination status |
|---|---|--|---|---|
| REVELAC-i | Regional SARI sentinel network | Children and elderly | PAHO/CDC case definition, respiratory samples taken ≤ 10 days, RT-PCR results only. | Immunised: Receipt of 1 dose >14 days prior to SARI symptoms onset. In children vaccinated for the first time, only able to assess partial immunization i.e. receipt of 1 dose. Ascertainment: EPI nominal registers, vaccination cards, and medical records. |
| I-MOVE multicentre case control study (Ireland, Germany, Hungary, Portugal, Romania, Spain) | Primary care sentinel networks | All age groups. GPs select patients to swab in a systematic way | EU case definition for ILI (swab taken <8 days after symptom onset). | Immunised: Receipt of 1 dose >15 days prior to ILI symptom onset. Ascertainment: medical registry or self-reported. |
| US/Flu VE Network case-control study | United States (Michigan, Pennsylvania, Texas, Washington, Wisconsin) Outpatient clinics | All age group Systematic recruitment of patients seeking outpatient medical care for ARI with cough, illness duration ≤ 7 days | Cases: Medically attended ARI and RT-PCR influenza Controls: Medically attended ARI but negative for influenza | Immunised: 1 dose ≥ 14 from illness onset (or 2 doses since 07/2010 for aged <9) Confirmed by medical record or registry |
| Canada | 100s of community-based practitioners from British Columbia, Alberta, Manitoba, Ontario and Quebec. | Patients presenting to a sentinel site within 7 days of ILI onset defined as acute onset of fever and cough and one or more of sore throat, arthralgia, myalgia or prostration | Eligible participants whose specimen tests positive for influenza; controls test negative for all influenza types/subtypes | Reported vaccine receipt 2 weeks or more prior to ILI onset |
| New Zealand (SHIVERS Hospital) | 2 hospitals in Auckland City | Population aged $> 6m$ hospitalised with influenza or pneumonia | Case: Hospitalised with PCR (92%) or viral culture (8%) confirmed influenza. Noncase: Next hospitalised adult with ILI but negative test for influenza (1:1) | Ascertainment: Self-reported. Immunised: 1 dose ≥ 14 days prior before date of admissions |
| Spain | Spanish Influenza Surveillance System (SISS) (17 primary care sentinel networks) | All age groups. Systematic swabbing of all patients over 64 years and of the first two patients less than 65 | EU case definition for ILI | Immunised: Receipt of 1 dose ≥ 15 days prior to ILI symptom onset Ascertainment: medical registry or self-reported |

Methods

- Set up the network of countries and collaborating agencies.
- Evaluation based on established SARI sentinel surveillance. All countries used regional standard definition for SARI (CDC-PAHO 2006 protocol)
- Common protocol, revised by countries. Submitted to national ethics committees
- Formed national working groups (influenza surveillance, expanded programs on immunization (EPI), reference laboratories and PAHO local offices-immunization focal points).

Methods

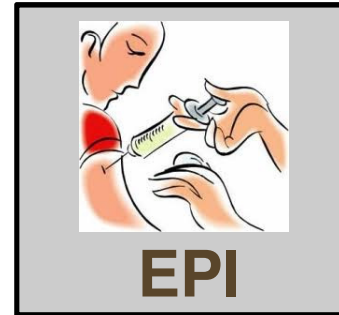
- Case-control (test-negative design)
- 1 Case: 3 Controls, identified through sentinel surveillance during April-December 2013, LAC influenza season.
Cases = SARI case-patients PCR-confirmed influenza
Controls = SARI case-patients PCR-negative for influenza
- Frequency matched by
 - Age-group (aged 6 months-5 yrs* or ≥ 60 yrs)
 - Epidemiological week of SARI onset
- Vaccination status: abstracted from surveillance and completed thru EPI (vaccination registries, vaccination cards, house visits).

* mostly <5 yrs, only 1 country up to 10 yrs with chronic dis.

Prospective data collection



During the influenza season (April – Sept/Dec)



SARI sentinel hospitals

1. Identification of potential case-patients:

- SARI (hospitalized)
- Children
- Older adults
- Respiratory sample

| Datos personales | datos sociodemograficos | enfermedades cronicas | Estado de vacunacion contra influenza | Resultado de Laboratorio |
|------------------|-------------------------|-----------------------|---------------------------------------|--------------------------|
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Ministerio de Salud - Caja de Seguro Social - Instituciones de Salud Privada
 Instituto Comunitario Gorgas de Estudios en Salud
 Formulario Para Vigilancia de la Influenza- Síndrome Gripal,
 Infecciones Respiratorias Agudas Graves-Bronconeumonías Virales y Bacterianas- Bronquiolitis

1. Instalación que notifica: AMBULATORIO () HOSPITALIZADO () FALLECIDO ()

2. Fecha de notificación:

3. Tipo de paciente:

4. Nombre: 1er Nombre, 2do nombre, Apellido paterno, Apellido materno

5. Ciudad, 6. Nº Hospital Clínico S.S., 7. Asegurado: S () No ()

8. Edad: Años, Meses, Días, 9. Fecha Nacimiento: Día, Mes, Año, 10. Sexo M () F ()

11. Dirección: Provincia, Región, Distrito, Corregimiento

12. Teléfono, 13. Número de la persona responsable

ANTECEDENTES:

14. Tipos de vacunas aplicadas: Sí () No ()

15. Tipo de vacuna: Sí () No ()

16. Fecha de vacunación: Día, Mes, Año

17. Síndrome respiratorio agudo: Sí () No ()

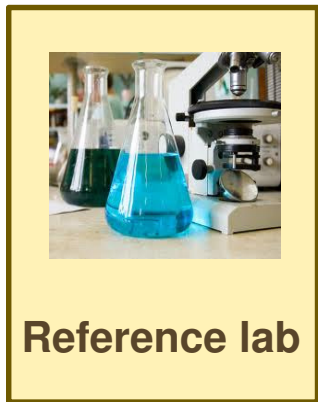
18. Síndrome respiratorio agudo confirmado: Sí () No ()

19. Tipo de contacto: Familiar () Social () Laboral ()

20. Nombre del contacto:

Vaccination cards

| Fecha | Nombre vacuna | Dosis | Observaciones |
|--------------|--------------------|--------|--|
| APR 2 3 2008 | HEPATITIS A | 1.0ml | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| APR 2 3 2008 | HEPATITIS B | 1.0ml | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| APR 2 3 2008 | TETANUS/DIPHTHERIA | 0.5 ml | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| APR 2 3 2008 | TETANUS | 0.5 ml | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| APR 2 3 2008 | POLIO | 0.5 ml | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| MAR 1 4 2008 | RABAVERT | 1.0ml | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| MAR 1 4 2008 | RABAVERT | 1.0ml | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| ABR 2 4 2008 | RABIES (MOVAV) | 1.0 ML | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |
| ABR 2 4 2008 | HEPATITIS B | 1.0 mL | REACTIVO POSITIVO PARA QUADRO NEGATIVO PARA QUADRO |



Reference lab

2. Follow-up for PCR result

- Flu (+) = case
- Flu (-) = controls

SARI case report forms

Data collection

Online regional database

SARI influenza surveillance system
or database

SARI influenza
surveillance forms

Direct upload from
existing systems

www.revelac-i.org

Data entry into
revelac-i interface

Critical variables

Age, sex

Date of symptoms onset, Date of sample
collection,

Current and previous year influenza vaccine
(dates, doses),

pneumococcal vaccine,

Antiviral treatment, preexisting conditions.

<http://173.201.187.40/revelac-i/revelac-i/data.php>

Vaccination status ascertainment

Exposure (seasonal influenza vaccination):

- Vaccinated = at least **14 days** vaccination–SARI onset.

SARI surveillance forms/databases

| 14. Tarjeta de vacuna: Si: <input type="checkbox"/> No: <input type="checkbox"/> No aplica: <input type="checkbox"/> | Aplicada | | N° de dosis aplicada | Fecha de última dosis | | |
|--|----------|----|----------------------|-----------------------|-----|-----|
| | Si | No | | Día | Mes | Año |
| 15. Tipo de vacuna | | | | | | |
| 15.1 Anti Influenza | | | | | | |
| 15.2 Anti H. Influenzae b | | | | | | |
| Anti Neumocócica | | | | | | |
| 15.3 Heptavalente | | | | | | |
| 15.4 23 valente | | | | | | |
| 15.5 Anti meningocócica (*) | | | | | | |
| (*)Especifique nombre de la vacuna: | | | | | | |

1. Improve completeness at hospital level and collect additional variables if necessary (ex.doses).

2. Complete vaccination data a posteriori

Matching patients by ID, name, age, address.

(other countries)

Computerized nominal immunization registry

(Chile, Colombia (1 region), Panama and Costa-Rica).

EPI registries at local level (nominal/paper, excel database), household visits/calls.

REVELAC-i - Enrollment in 2013

| influenza status | region | | Total |
|---------------------|-----------|-----------|--------|
| | Central-A | South Ame | |
| control | 92 | 1,276 | 1,368 |
| | 6.73 | 93.27 | 100.00 |
| case | 45 | 402 | 447 |
| | 10.07 | 89.93 | 100.00 |
| Total | 137 | 1,678 | 1,815 |
| | 7.55 | 92.45 | 100.00 |

Data received as of Febr. 28 2014

Influenza vaccine status ascertainment using existing EPI data sources

| | Countries with nominal vaccination registries* | Countries with no vaccinations registries# |
|---------------------------------------|--|--|
| Completeness of information | | |
| Current influenza vaccination status | 1054/1065 (99%) | 327/447 (73%) |
| Among children | 330/335 (99%) | 158/205 (77%) |
| Among elderly | 724/730 (99%) | 169/242 (70%) |
| Receipt of 2nd dose in children<9 yrs | 311/332 (94%) | 148/205 (72%) |
| Previous season influenza vaccination | 845/1065 (79%) | 318/447 (71%) |
| Vaccination coverage (2013) | | |
| Children | 62% | 47% |
| Elderly | 51% | 17% |

*Chile, Colombia (Bogota), Panama (varying geographic coverage) and Costa Rica.

Included field work to retrieve information from vaccination cards and local records.

Data received as of Febr. 28 2014

Next steps for information systems supporting REVELAC-i

- To ensure the sustainability of estimating influenza VE annually, it is essential to **improve nominal vaccination registries** and including the **elderly** and other high risk groups
- Current SARI surveillance databases/systems should include the critical **vaccination variables** to estimate vaccine effectiveness (**update of the PAHO/CDC regional SARI surveillance protocol ongoing**)
- Explore **existing country databases** or **other regional databases** to conduct further influenza VE evaluations using **other study designs (for eg. Cohort studies)** or using different disease outcomes (ex. Influenza-like illness, Perinatal Clinical History - CLAP).

REVELAC-i

Red para la **Evaluación** de la **Efectividad** de la **Vacuna**
En **Latino América** y el **Caribe** – *influenza*



Antigua - Guatemala. 27 February 2013

<http://www.paho.org/revelac-i/>



**Second REVELAC-i meeting,
Cartagena, Colombia
26-28 March 2014**

Acknowledgments

- LAC Countries
 - In particular, immunization programs, surveillance and laboratories teams
- PAHO: Immunization, CLAP, WHO
- Partners (CDC, TEPHINET)
- I-MOVE (European Network for Influenza VE)