GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	An observational, retrospective, database study of the burden of seasonal Influenza A and B in Panama, selected countries of Central America and the Caribbean from the Year 2010 to 2015.
eTrack study number and Abbreviated Title	205049 (EPI-FLU-052 BOD PA DB)
Scope:	All data pertaining to the above study.
Date of Statistical Analysis Plan	20-Sep-2017
Co-ordinating author:	PPD (Statistician)
Reviewed by:	PPD (Regional Epidemiologist) PPD (Director Epidemiology) PPD (Lead statistician) PPD (Lead statistical analyst) PPD (Scientific writer) PPD (Public disclosure representative) PPD (stat peer reviewer)
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APP 9000058193 Statistical Analysis Plan Template (Effective date: 14 April 2017)

TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

LIST OF TEMPLATES

PAGE

LIST OF ABBREVIATIONS

CI	Confidence Interval
CTRS	Clinical Trial Registry Summary
DB	Database
GSK	GlaxoSmithKline
ICGES	Instituto Conmemorativo Gorgas de Estudios de la Salud
LL	Lower Limit of the confidence interval
N.A.	Not Applicable
SAP	Statistical Analysis Plan
SD	Standard Deviation
SLIPE	Sociedad Latinoamericana de Infectología Pediátrica
SR	Study Report
TFL	Tables Figures and Listings
TIV	Trivalent Influenza Vaccines
TOC	Table of Content
UL	Upper Limit of the confidence interval

1. DOCUMENT HISTORY

Date	Description	Protocol Version
20-SEP-2017	Final version	Final Version 1: 29 March 2016

2. STUDY DESIGN

- Type of study: Self-contained.
- Type of design: Epidemiological, non-interventional, observational, retrospective, database study.
- Study population: All subjects who have laboratory confirmed diagnosis of influenza (laboratory confirmed case) and reported in the national influenza surveillance system in selected countries from the Year 2010-2015.
- General study aspects: All seasonal influenza A and/or B cases reported in the ICGES database will be screened. Demographic data, date of onset of the first symptom and data on A-virus subtype and B-strain lineage, geographic region where the virus was isolated, clinical features and outcomes (clinical symptoms, duration of illness, complications) experienced by all influenza positive subjects (subjects with a laboratory confirmed influenza diagnosis) will be validated, extracted and transferred from the ICGES database to the sponsor or to the site of analysis, as applicable.
- Period of data collection: The study will include data on all the subjects with a laboratory confirmed influenza diagnosis, reported in the ICGES database of Panama, from January 2010 to December 2015. For all eligible subjects, individual level anonymised and key coded data will be collected from the database.
    - Epoch 001: Retrospective data collection.

Table 1 Study group and epoch foreseen in the study

Study Group	Epoch
	Epoch 001
Retrospective	x

3. OBJECTIVES

3.1. Primary objective

- To describe seasonal influenza A and/or B cases by age and virus subtype (AH1N1/A H3N2) and B-strain lineage (Victoria and Yamagata) using data reported via National Surveillance Program in Panama, selected countries of Central America and the Caribbean from January 2010 to December 2015.

3.2. Secondary objectives

From January 2010 to December 2015, in each selected country:

- To describe clinical features and outcomes (clinical manifestations, duration of illness, complications) of seasonal Influenza A and B cases in (overall and by subtypes or lineages) different seasons.
- To describe the temporal and geographical distribution of seasonal influenza A and/or B (overall and by subtypes or lineages) cases within different seasons.
- To estimate the percentage of co-circulation of influenza B lineages (Yamagata and Victoria lineages) among the study population, by age categories and by region.
- To describe the mismatch between the B-strain included in the Trivalent Influenza Vaccines (TIV) and the circulating B strains in different seasons.

4. ENDPOINTS

4.1. Primary endpoint

- Occurrence of seasonal influenza A and/or B cases by age, virus subtype and strain lineage from the January 2010 to December 2015, in Panama, selected countries of Central America and the Caribbean (using the data reported via National Influenza Surveillance Program).

4.2. Secondary endpoints

- Occurrence of clinical features and outcomes (clinical symptoms, duration of illness, complications) experienced by subjects who have laboratory confirmed diagnosis seasonal influenza A and/or B, in different seasons from 2010 to 2015.
- Frequency of seasonal influenza A and/or B cases reported in different temporal and geographical locations within different seasons from 2010 to 2015.
- Occurrence of influenza caused by B-strain and presented by B lineages among the study population, by age (<1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-44, 45-49, 50-59, 60-64 and ≥ 65 years) and by region.
- Compare the characteristics of the influenza B-infection as observed in the database and the B-strain included in the trivalent influenza vaccine.

5. ANALYSIS SETS

5.1. Definition

5.1.1. Screened cohort

The screened cohort will include all the specimen samples received per year within the ICGES influenza surveillance system for influenza testing at aggregated level

5.1.2. Total cohort

The Total cohort will comprise of all eligible subjects included in the study.

5.2. Criteria for eliminating data from Analysis Sets

Not applicable for database studies

6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in annex 1 and will not be repeated below.

All the analysis on primary and secondary objectives will be performed on Total cohort.

6.1. Demography

6.1.1. Analysis of demographics/baseline characteristics planned in the protocol

Demographic characteristics (age and gender) will be summarised by group using descriptive statistics:

- Frequency tables will be generated for categorical variable such as gender.
- Mean, median and standard deviation will be provided for continuous data such as age.
- The distribution of influenza cases by month and year will also be tabulated.

6.1.2. Additional considerations

Number of specimen samples received per year within the ICGES influenza surveillance system for influenza testing will be tabulated using frequency and percentages by calendar year and by Southern Hemisphere/Northern Hemisphere influenza season

6.2. Primary objective

6.2.1. Analysis of primary objective planned in the protocol

The proportion of subjects with influenza caused by seasonal influenza A and/or B among all influenza cases reported with exact 95% confidence interval (CI) by age, A-virus subtype and B-strain lineage and overall will be calculated.

6.2.2. Additional considerations

None

6.3. Secondary objectives

6.3.1. Analysis of secondary objectives planned in the protocol

Seasonal influenza A and/or B cases will be described using frequency and percentages by temporal (calendar weeks/months) and geographical distributions (by country and by region within the country [if data is available]) within different influenza seasons (2010-2011, 2011-2012, 2012-2013, 2013-2014 and 2014-2015). Frequency and percentage for clinical features and outcomes (clinical manifestations, duration of illness, complications) experienced by influenza positive subjects will be tabulated by type of influenza (seasonal influenza A and/or B) in different seasons from 2010-2015. Frequency and percentage for influenza B lineages by age (<1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-44, 45-49, 50-59, 60-64 and ≥ 65 years) and region will also be provided.

The characteristics of the influenza B-infection as observed in the database and the B strain included in the trivalent influenza vaccine will be assessed using frequency and percentage for each year. The proportion of matched B-strains and mis-matched B-strains will be estimated along with 95% CI.

6.3.2. Additional considerations

Influenza A and/or B specimens (overall and by subtypes or lineages) will be described using frequency and percentages by country as well as Southern Hemisphere or Northern Hemisphere influenza season (depending which hemisphere influenza season the country follows). Example: Panama, El Salvador, Trinidad are considered as southern hemisphere and Guatemala, Dominican republic as northern hemisphere.

The proportion of mismatched B lineage will be calculated as 1 minus proportion of matched B lineage and expressed as percentages.

7. ANALYSIS INTERPRETATION

All the analyses with respect to the primary and secondary endpoints will be descriptive. These descriptive analyses will not be interpreted, except describing the study results.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

There will be an interim analysis perform on available data (lab database for Panama) to submit the abstract/poster to SLIPE congress with preliminary results. The final analysis will be performed when all required data for the study have been extracted from the ICGES database and transferred to the sponsor or to the site of analysis, as applicable.

Description	**Analysis ID**	**Disclosure Purpose (CTRS=public posting, SR=study report, internal)**	**Dry run review needed (Y/N)**	***Study Headline Summary (SHS)*requiring expedited communication to upper management (Yes/No)**	**Reference for TFL**
Analysis for abstract/poster submission to SLIPE congress	E1_01	Abstract/poster submission	N	No	TFL TOC-Abstract/poster submission (column J)
Final Analysis of epoch 1	E1_02	SR, CTRS	N	Yes	TFL TOC - All TFLs

8.2. Statistical considerations for interim analyses

All the analyses with respect to the primary and secondary endpoints will be descriptive/ exploratory. As the results of the interim analyses will not be used to alter the study conduct, no statistical adjustment for interim analyses is required.

9. CHANGES FROM PLANNED ANALYSES

- There will be an interim analysis planned on available data (lab database for Panama) in order to submit the abstract\poster for SLIPE congress
- We will also be reporting the number of specimen samples received per year within the ICGES influenza surveillance system for influenza testing at aggregated level (considered as screened cohort) and determine the proportion that tested positive for Influenza to describe the reporting capabilities of the surveillance system at capturing influenza A and B cases.
- We will also be including seasonal 2016 data as it is presently available. Based on the dates of data transfer, the end time period may be expanded if data is available during data transfer
- All the statistical analysis will be performed on specimens instead of subjects because a subject can provide more than one influenza positive specimens.
- The age group used for the analysis are 0-4, 5-17, 18-49, 50-64 and >=65 years instead of <1, 1-4, 5-9, 10-14, 15-19, 20-24, 25-44, 45-49, 50-59, 60-64 and ≥ 65 years.

10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures needed for the study report. It also identifies the tables eligible for each analyses and their role (synopsis, in-text, post-text, SHS, CTRS). Note that all TFL aimed to be included as post-text are noted as post-text even if these are tabulation of individual data such as listing of SAE. The post-text material contains all source material for the study report and accordingly a post-text table may be redundant with an in-text table.

The mock tables referred under column named 'layout' can be found in PPD dedicated folder for standard tables and in Annex 3 for study specific mock table/figure/listing. The latter table/figure/listing are identified by the prefix SS_ in the TFL Toc.

The following group names will be used in the TFLs:

Group order in tables	Group label in tables	Group definition for footnote
PP	Influenza A	Positive for Influenza A
PP	Influenza B	Positive for Influenza B
Or/and		
PP	H1N1	Positive for Influenza A subtype H1N1
PP	H3N2	Positive for Influenza A subtype H3N2
Or/and		
PP	Victoria	Positive for Influenza B lineage Victoria
PP	Yamagata	Positive for Influenza B lineage Yamagata
Or/and		
PP	0-4	0-4 years of age
PP	5-17	5-17 years of age
PP	18-49	18-49 years of age
PP	50-64	50-64 years of age
PP	>=65	>=65 years of age
Or/and		
PP	West	West: Boca del Toro, Chiriquí and Comarca Nobe Bugle
PP	Central	Central: Coclé, Herrera, Los Santos and Veraguas
PP	Panama	Panamá: Panamá Este, Panamá Oeste, Panamá Metro and San Miguelito
PP	Northeast	Northeast: Colón, Darien and Kuna Yala

Influenza season		
Calendar year (Jan-Dec)	**Southern Hemisphere (May-Oct)**	**Northern Hemisphere (Oct-May)**
Jan-Dec 2010	May– Oct 2010	Oct 2010-May 2011
Jan-Dec 2011	May– Oct 2011	Oct 2011-May 2012
Jan-Dec 2012	May– Oct 2012	Oct 2012-May 2013
Jan-Dec 2013	May– Oct 2013	Oct 2013-May 2014
Jan-Dec 2014	May– Oct 2014	Oct 2014-May 2015
Jan-Dec 2015	May– Oct 2015	Oct 2015-May 2016
Jan-Dec 2016	May– Oct 2016	Oct 2016-May 2017

11. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

11.1. Statistical Method References

- The exact two-sided 95% CIs for a proportion within a group will be the Clopper-Pearson exact CI [Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika*. 1934;26:404-413].
- WHO recommendations on the composition of influenza virus vaccines by influenza season can be found under: http://www.who.int/influenza/vaccines/virus/recommendations/en/

11.2. Standard data derivation GSK legacy

11.2.1. Date derivation

- SAS date derived from a character date: In case day is missing, 15 is used. In case day & month are missing, 30June is used.

11.2.2. Demography

- Age at date of onset of the first symptom, will be expressed in years in the study. This will be computed as the difference between the date of onset of the first symptom and the date of birth (only if the data is available).
- The percentages will be computed by using only available information. Only frequencies will be provided for unknown or missing or not applicable categories
- Any measurements omitted or non-evaluable for a particular subject or analysis will not be replaced. Therefore, subjects with omitted or non-evaluable measurements will be excluded from the analysis

11.2.3. Case definition

- Influenza is defined as any positive laboratory test from one or more of the clinical specimens [Guidelines for the epidemiological surveillance of influenza, 2012].

11.2.4. Number of decimals displayed:

The following decimal description from the decision rules will be used

Display Table	Parameters	Number of decimal digits
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	1
All summaries	% of count, including LL & UL of CI	1

12. ANNEX 2: SUMMARY ON ELIMINATION CODES

Not Applicable

13. ANNEX 3: STUDY SPECIFIC MOCK TFL

The following drafted study specific mocks will be used for each country (Panama, El Salvador, Guatemala and Trinidad, Dominican Republic, etc.,)

The data display, title and footnote is for illustration purpose and will be adapted to the study specificity as indicated in the TFL TOC.

Some these templates were copied from EPI-FLU-032 BOD MX DB (201075) study. Note that there may be few changes between the study specific SAP mock TFL and the final TFLs as editorial/minor changes do not require a SAP amendment

Template 1 Number of specimen samples by calendar year - <country> (Screened cohort)

	Total specimen samples received	Respiratory virus positive		Influenza virus positive		Influenza A positive		Influenza B positive	
Year	N	n	%	n	%		%	n	%
Jan-Dec 2010									
Jan-Dec 2011									
Jan-Dec 2012									
Jan-Dec 2013									
Jan-Dec 2014									
Jan-Dec 2015									
Jan-Dec 2016									
Total									

N =total number of specimen samples received
n = number of positive specimen in a given category
%=(n/N)*100

Figure 1 Distribution of influenza positive specimens among number of specimen samples tested by calendar year - <country> (Screened cohort)

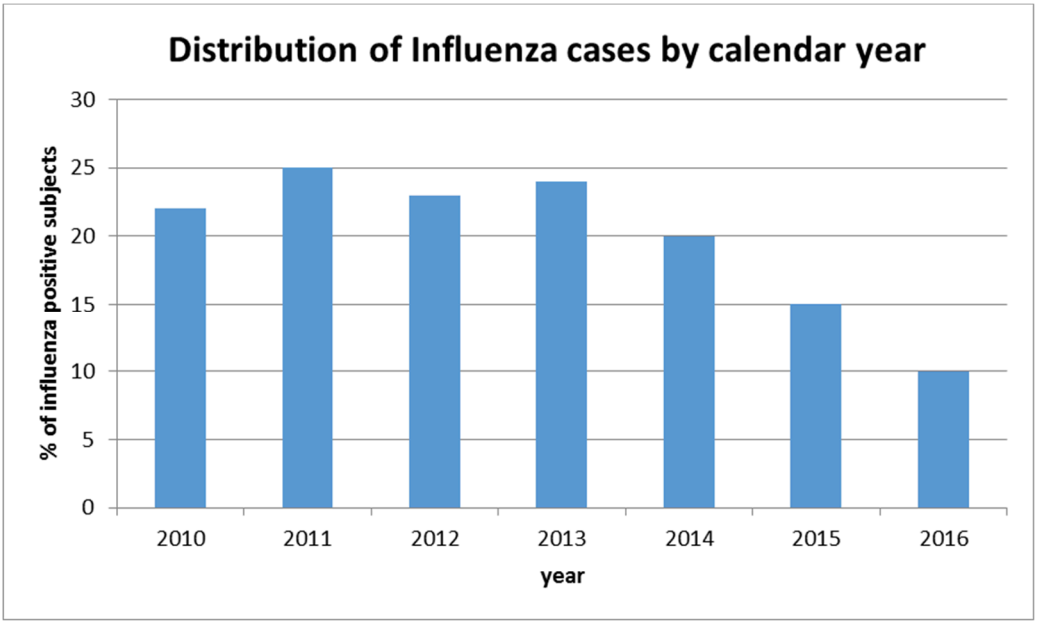
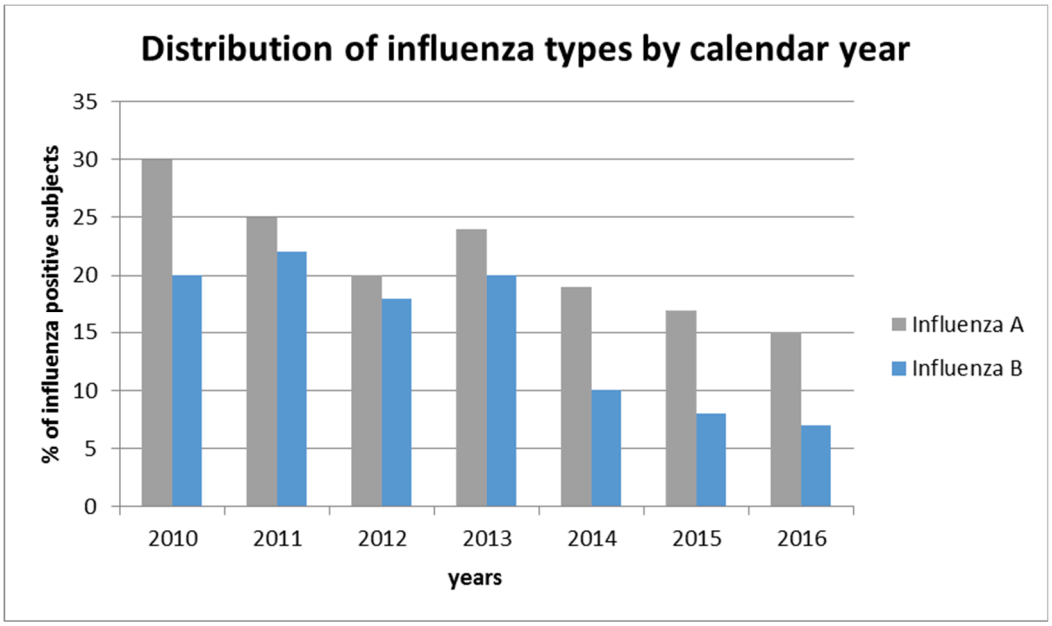


Figure 2 **Distribution of influenza types among number of specimen samples tested by calendar year - <country> (Screened cohort)**



Template 2 **Number of specimen samples by influenza season - <country> (Screened cohort)**

	Total specimen samples received	Respiratory virus positive		Influenza virus positive		Influenza A positive		Influenza B positive	
<Southern/northern hemisphere influenza season>	N	n	%	n	%		%	n	%
May– Oct 2010									
May– Oct 2011									
May– Oct 2012									
May– Oct 2013									
May– Oct 2014									
May– Oct 2015									
May– Oct 2016									
Total									

N =total number of specimen samples received
n = number of positive specimens in a given category
%=(n/N)*100

Figure 3 **Distribution of influenza positive specimens among number of specimen samples tested by influenza season - <country> (Screened cohort)**

Refer to Figure 1

Figure 4 **Distribution of influenza types among number of specimen samples tested by influenza season - <country> (Screened cohort)**

Refer to Figure 2

Template 3 Summary of demographic characteristics by influenza types - <country> (Total cohort)

		Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age [Years]	n		-		-		-
	Mean		-		-		-
	SD		-		-		-
	Median		-		-		-
	Minimum		-		-		-
	Maximum		-		-		-
	Missing		-		-		-
Age group [Years]	0-4						
	5-17						
	18-49						
	50-64						
	>=65						
	Missing		-		-		-
Gender	Female						
	Male						
Region	West						
	Central						
	Panama						
	Northeast						
Patient type	Outpatient						
	Hospitalized						

N = number of influenza positive specimens
n = number of specimen positive in a given category
% = n / Number of specimens with available results x 100
Value = value of the considered parameter
SD = Standard deviation
West: Boca del Toro, Chiriquí and Comarca Nobe Bugle
Central: Coclé, Herrera, Los Santos and Veraguas
Panamá: Panamá Este, Panamá Oeste, Panamá Metro and San Miguelito
Northeast: Colón, Darien and Kuna Yala

Template 4 Summary of demographic characteristics by influenza A subtypes and B lineages - <country> (Total cohort)

		Influenza A subtypes				Influenza B lineage			
		H1N1 N=XX		H3N2 N=XX		Victoria N=XX		Yamagata N=XX	
Characteristics	**Parameters or Categories**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**	**Value or n**	**%**
Age [Years]	n		-		-				-
	Mean		-		-				-
	SD		-		-				-
	Median		-		-				-
	Minimum		-		-				-
	Maximum		-		-				-
	Missing		-		-				-
Age group [Years]	0-4								
	5-17								
	18-49								
	50-64								
	>=65								
	Missing		-		-				-
Gender	Female								
	Male								
Region	West								
	Central								
	Panama								
	Northeast								
Patient type	Outpatient								
	Hospitalized								

N = number of influenza positive specimens
n = number of specimen positive in a given category
% = n / Number of specimens with available results x 100
Value = value of the considered parameter
SD = Standard deviation
West: Boca del Toro, Chiriquí and Comarca Nobe Bugle
Central: Coclé, Herrera, Los Santos and Veraguas
Panamá: Panamá Este, Panamá Oeste, Panamá Metro and San Miguelito
Northeast: Colón, Darien and Kuna Yala

Template 5 Distribution of influenza A cases by month and year - <country> (Total cohort)

Month and year (date of onset of symptoms)	Influenza virus positive (N)	Influenza A positive (n)	Percentage (%)
Jan2010			
Feb2010			
Mar 2010			
Apr2010			
May2010			
Jun2010			
Jul2010			
Aug2010			
Sep2010			
Oct2010			
Nov2010			
Dec2010			
Jan2011			
Feb2011			
….			
Dec2016			

N = number of influenza positive specimens with available test results by month and year
n = number of influenza A positive specimen in a given category
% = (n / N) x 100

Template 6 Distribution of influenza B cases by month and year - <country> (Total cohort)

Refer to Template 5

Template 7 Distribution of influenza A subtype H1N1 cases by month and year - <country> (Total cohort)

Month and year (date of onset of symptoms)	Influenza virus positive (N)	Influenza A subtype H1N1 (n)	Percentage (%)
Jan2010			
Feb2010			
Mar 2010			
Apr2010			
May2010			
Jun2010			
Jul2010			
Aug2010			
Sep2010			
Oct2010			
Nov2010			
Dec2010			
Jan2011			
Feb2011			
….			
Dec2016			

N = number of influenza positive specimens with available test results by month and year
n = number of influenza A subtype H1N1 specimens in a given category
% = (n / N) x 100

Template 8 Distribution of influenza A subtype H3N2 cases month and year - <country> (Total cohort)

Refer to Template 7

Template 9 Distribution of influenza B lineage Victoria cases by month and year - <country> (Total cohort)

Month and year (date of onset of symptoms)	Influenza virus positive (N)	Influenza B lineage Victoria (n)	Percentage (%)
Jan2010			
Feb2010			
Mar 2010			
Apr2010			
May2010			
Jun2010			
Jul2010			
Aug2010			
Sep2010			
Oct2010			
Nov2010			
Dec2010			
Jan2011			
Feb2011			
….			
Dec2016			

N = number of influenza positive specimens with available test results by month and year
n = number of Influenza B lineage Victoria specimens in a given category
% = (n / N) x 100

Template 10 Distribution of influenza B lineage Yamagata cases by month and year - <country> (Total cohort)

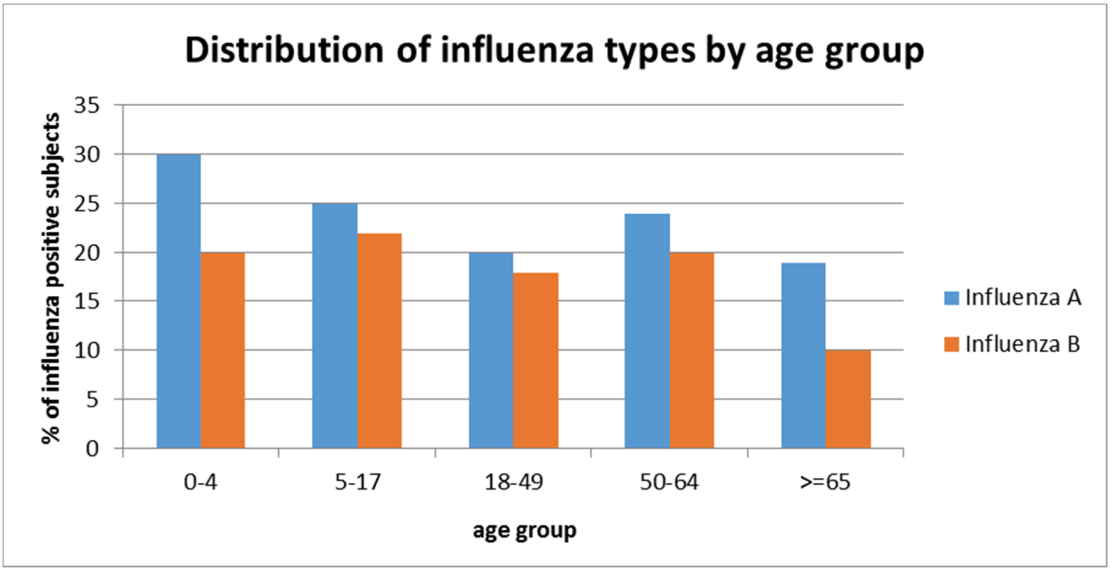
Refer to Template 9

Template 11 Summary of influenza types by age group - <country> (Total cohort)

		0-4 N=XX				5-17 N=XX				… N=XX				Total N=XX			
Influenza type	Categories	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL			LL	UL
Influenza A	Positive																
	Negative																
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-
Influenza B	Positive																
	Negative																
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-
Influenza A and B	Both Positive																
	Both Negative																
	At least one positive																
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-

N = number of influenza positive specimens by age group
n = number of specimens in a given category
% = n / Number of specimens with available results x 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Figure 5 Distribution of influenza types by age group - <country> (Total cohort)

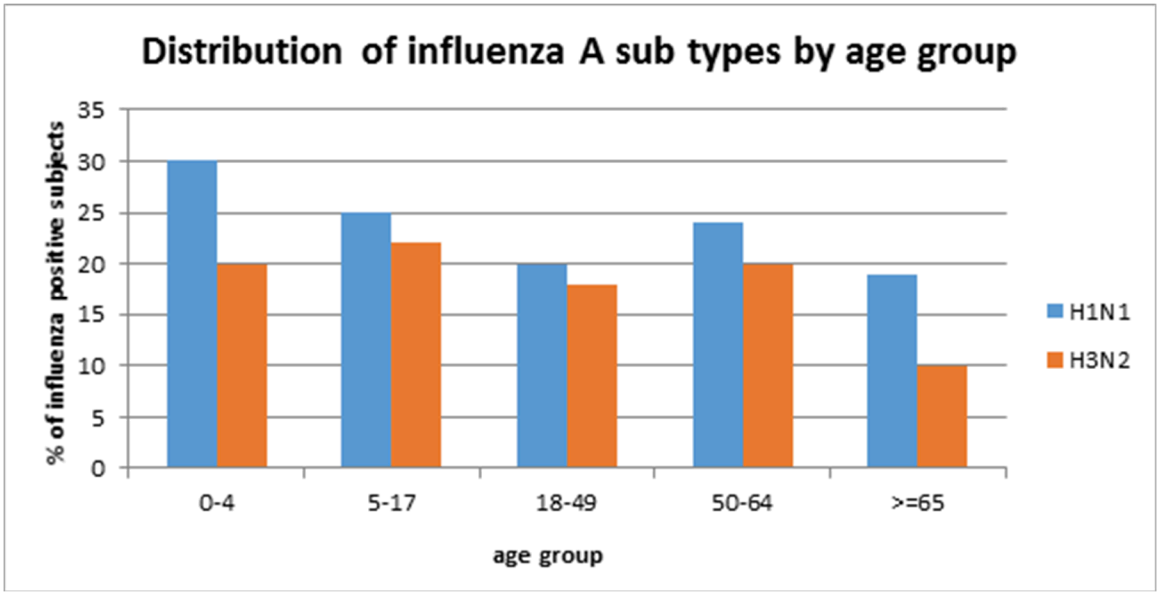


Template 12 Summary of influenza A subtypes by age group - <country> (Total cohort)

		0-4 N=XX				5-17 N=XX				... N=XX				Total N=XX			
Influenza A sub-type	Categories	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL			LL	UL
H1N1	Positive																
	Negative																
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-
H3N2	Positive																
	Negative																
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-

N = number of influenza positive specimens by age group
n = number of specimens in a given category
% = n / Number of specimens with available results x 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Figure 6 Distribution of influenza A sub types by age group - <country> (Total cohort)

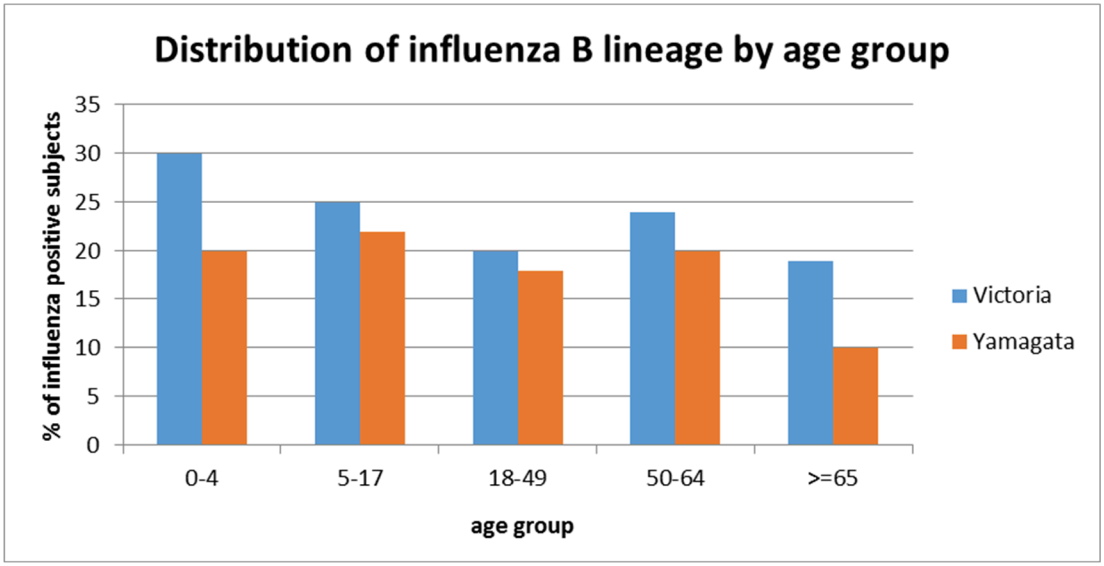


Template 13 Summary of influenza B lineage by age group - <country> (Total cohort)

		0-4 N=XX				5-17 N=XX				... N=XX				Total N=XX			
Influenza B lineage	Categories	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL			LL	UL
Victoria	Positive																
	Negative																
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-
Yamagata	Positive																
	Negative																
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-

N = number of influenza positive specimens by age group
n = number of specimens in a given category
% = n / Number of specimens with available results x 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Figure 7 Distribution of influenza B lineage by age group - <country> (Total cohort)

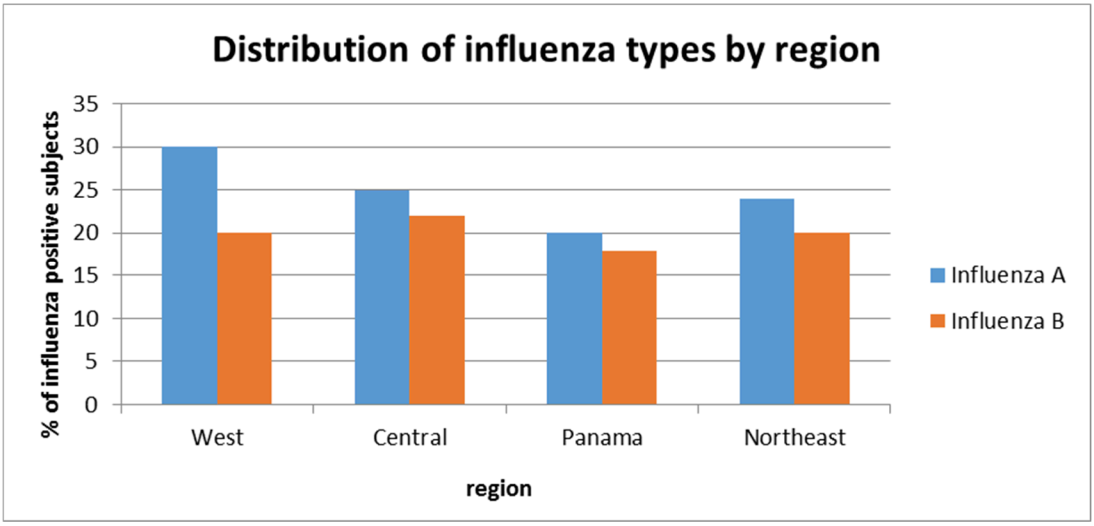


Template 14 Summary of influenza types by region - <country> (Total cohort)

		West N=XX				Central N=XX				Panama N=XX				Northeast N=XX				Total N=XX			
Influenza type	Categories	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL			LL	UL			LL	UL
Influenza A	Positive																				
	Negative																				
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-
Influenza B	Positive																				
	Negative																				
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-
Influenza A and B	Both Positive																				
	Both Negative																				
	At least one positive																				
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-

N = number of influenza positive specimens by region
n = number of specimens in a given category
% = n / Number of specimens with available results x 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit
West: Boca del Toro, Chiriquí and Comarca Nobe Bugle
Central: Coclé, Herrera, Los Santos and Veraguas
Panamá: Panamá Este, Panamá Oeste, Panamá Metro and San Miguelito
Northeast: Colón, Darien and Kuna Yala

Figure 8 Distribution of influenza types by region - <country> (Total cohort)

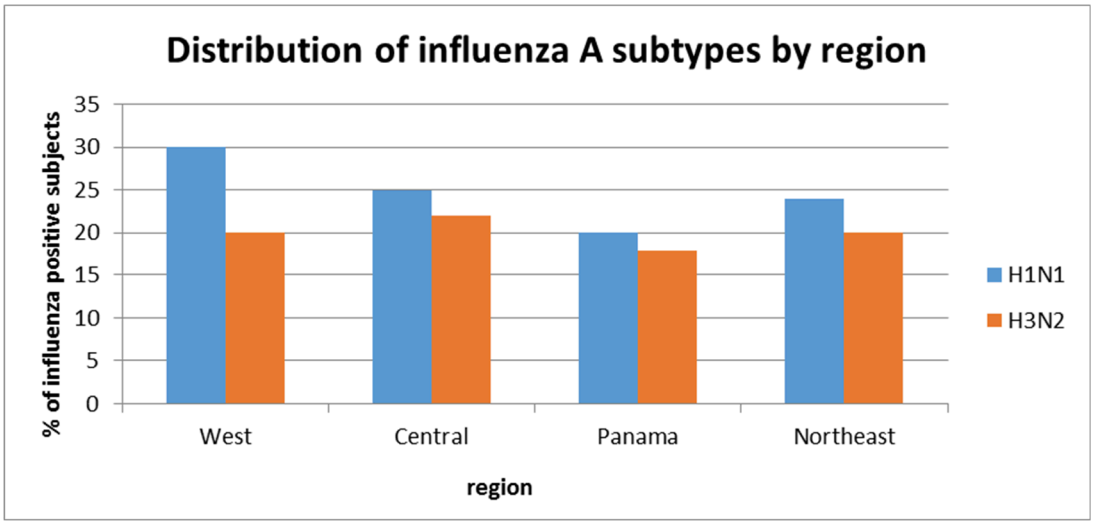


Template 15 Summary of influenza A subtypes by region - <country> (Total cohort)

		West N=XX				Central N=XX				Panama N=XX				Northeast N=XX				Total N=XX			
Influenza A subtypes	Categories	n	%	95% CI		N	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL			LL	UL			LL	UL
H1N1	Positive																				
	Negative																				
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-
H3N2	Positive																				
	Negative																				
	Missing/Unknown		-	-	-		-	-	-		-	-	-		-	-	-		-	-	-

N = number of influenza positive specimens by age group
n = number of specimens in a given category
% = n / Number of specimens with available results x 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit
West: Boca del Toro, Chiriquí and Comarca Nobe Bugle
Central: Coclé, Herrera, Los Santos and Veraguas
Panamá: Panamá Este, Panamá Oeste, Panamá Metro and San Miguelito
Northeast: Colón, Darien and Kuna Yala

Figure 9 Distribution of influenza A subtypes by region - <country> (Total cohort)

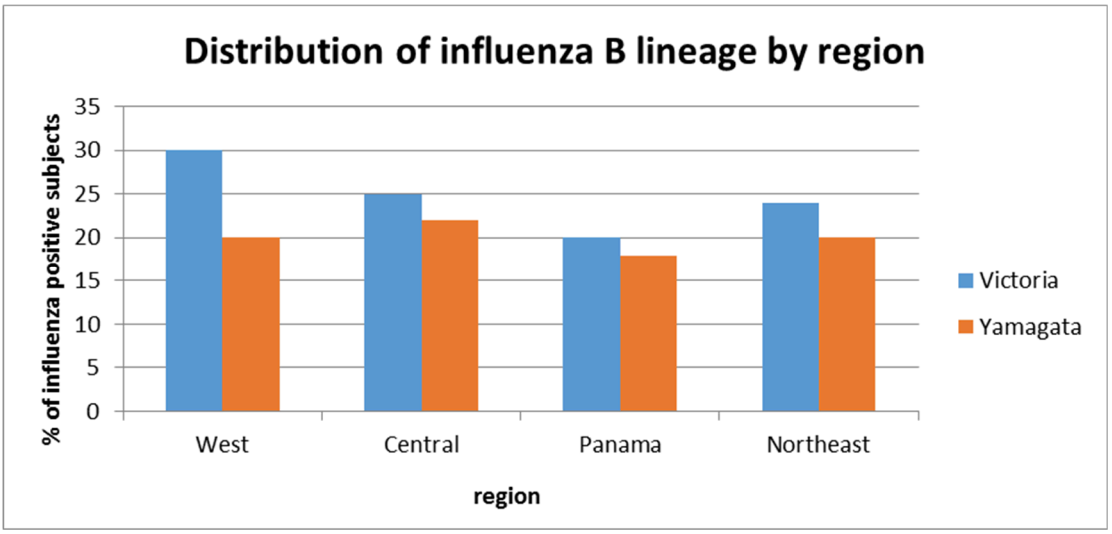


Template 16 Summary of influenza B lineage by region - <country> (Total cohort)

		West N=XX				Central N=XX				Panama N=XX				Northeast N=XX				Total N=XX			
Influenza B lineage	Categories	n	%	95% CI		N	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
				LL	UL			LL	UL			LL	UL			LL	UL			LL	UL
Victoria	Positive																				
	Negative																				
	Missing/Unknown		-	-	-		-	-	-		-	-	-						-	-	-
Yamagata	Positive																				
	Negative																				
	Missing/Unknown		-	-	-		-	-	-		-	-	-						-	-	-

N = number of influenza positive specimens by age group
n = number of specimens in a given category
% = n / Number of specimens with available results x 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit
West: Boca del Toro, Chiriquí and Comarca Nobe Bugle
Central: Coclé, Herrera, Los Santos and Veraguas
Panamá: Panamá Este, Panamá Oeste, Panamá Metro and San Miguelito
Northeast: Colón, Darien and Kuna Yala

Figure 10 Distribution of influenza B lineage by region - <country> (Total cohort)



Template 17 Proportion of Influenza caused by influenza A and/or B among all influenza cases by calendar year - <country> (Total cohort)

					95% CI	
Calendar year	**Influenza type**	**n**	**N**	**%**	**LL**	**UL**
2010	Influenza A					
	Influenza B					
2011	Influenza A					
	Influenza B					
2012	Influenza A					
	Influenza B					
2013	Influenza A					
	Influenza B					
2014	Influenza A					
	Influenza B					
2015	Influenza A					
	Influenza B					
2016	Influenza A					
	Influenza B					
Total	Influenza A					
	Influenza B					

N = Number of Influenza positive specimens with available test results by year
n = Number of positive specimens in a given category
% = (n/N) * 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Template 18 Proportion of Influenza caused by influenza A and/or B among all influenza cases by influenza season - <country> (Total cohort)

					95% CI	
<Southern/northern hemisphere Influenza season>	**Influenza type**	**n**	**N**	**%**	**LL**	**UL**
May– Oct 2010	Influenza A					
	Influenza B					
May– Oct 2011	Influenza A					
	Influenza B					
May– Oct 2012	Influenza A					
	Influenza B					
May– Oct 2013	Influenza A					
	Influenza B					
May– Oct 2014	Influenza A					
	Influenza B					
May– Oct 2015	Influenza A					
	Influenza B					
May– Oct 2016	Influenza A					
	Influenza B					
Total	Influenza A					
	Influenza B					

N = Number of Influenza positive specimens with available test results by year
n = Number of positive specimens in a given category
% = (n/N)* 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Figure 11 Distribution of Influenza caused by influenza A and/or B among all influenza cases by calendar year - <country> (Total cohort)

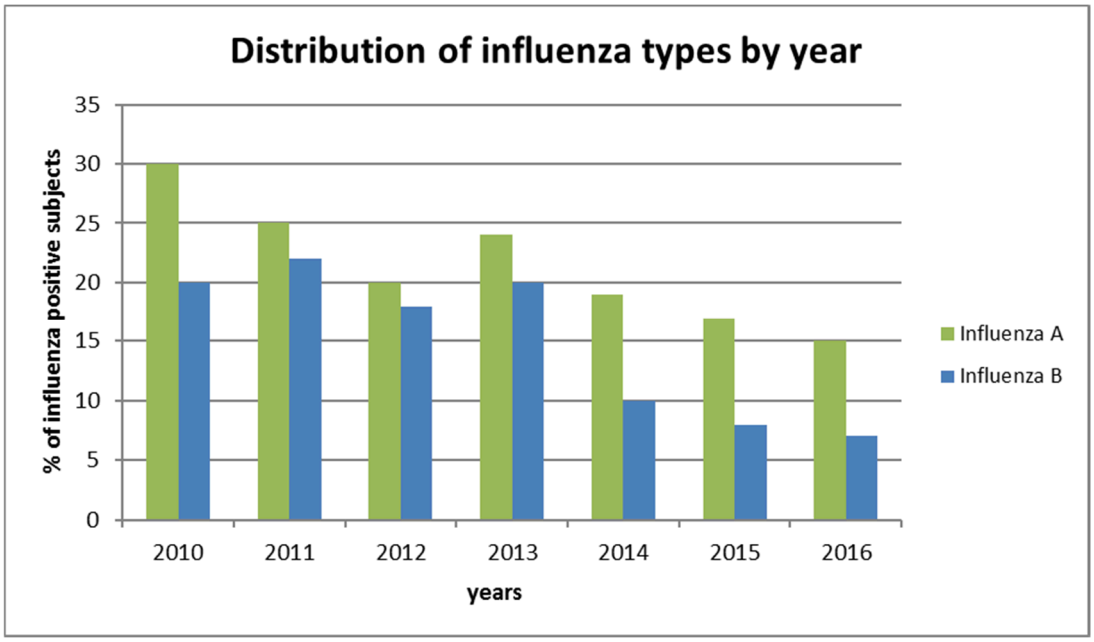


Figure 12 Distribution of Influenza caused by influenza A and/or B among all influenza cases by influenza season - <country> (Total cohort)

Refer to Figure 11

Template 19 Proportion of Influenza A subtypes among all influenza cases by calendar year - <country> (Total cohort)

					95% CI	
Year	**Influenza A subtypes**	**n**	**N**	**%**	**LL**	**UL**
2010	H1N1					
	H3N2					
2011	H1N1					
	H3N2					
2012	H1N1					
	H3N2					
2013	H1N1					
	H3N2					
2014	H1N1					
	H3N2					
2015	H1N1					
	H3N2					
2016	H1N1					
	H3N2					
Total	H1N1					
	H3N2					

N = Number of Influenza positive specimens with available test results by year
n = Number of positive specimens in a given category
% = n/N * 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Template 20 Proportion of Influenza A subtypes among all influenza cases by influenza season - <country> (Total cohort)

					95% CI	
<Southern/northern hemisphere influenza season>	Influenza A subtypes	n	N	%	LL	UL
May– Oct 2010	H1N1					
	H3N2					
May– Oct 2011	H1N1					
	H3N2					
May– Oct 2012	H1N1					
	H3N2					
May– Oct 2013	H1N1					
	H3N2					
May– Oct 2014	H1N1					
	H3N2					
May– Oct 2015	H1N1					
	H3N2					
May– Oct 2016	H1N1					
	H3N2					
Total	H1N1					
	H3N2					

N = Number of Influenza positive specimens with available test results by year
n = Number of positive specimens in a given category
% = n/N * 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Figure 13 Distribution of Influenza A subtypes among all influenza cases by calendar year - <country> (Total cohort)

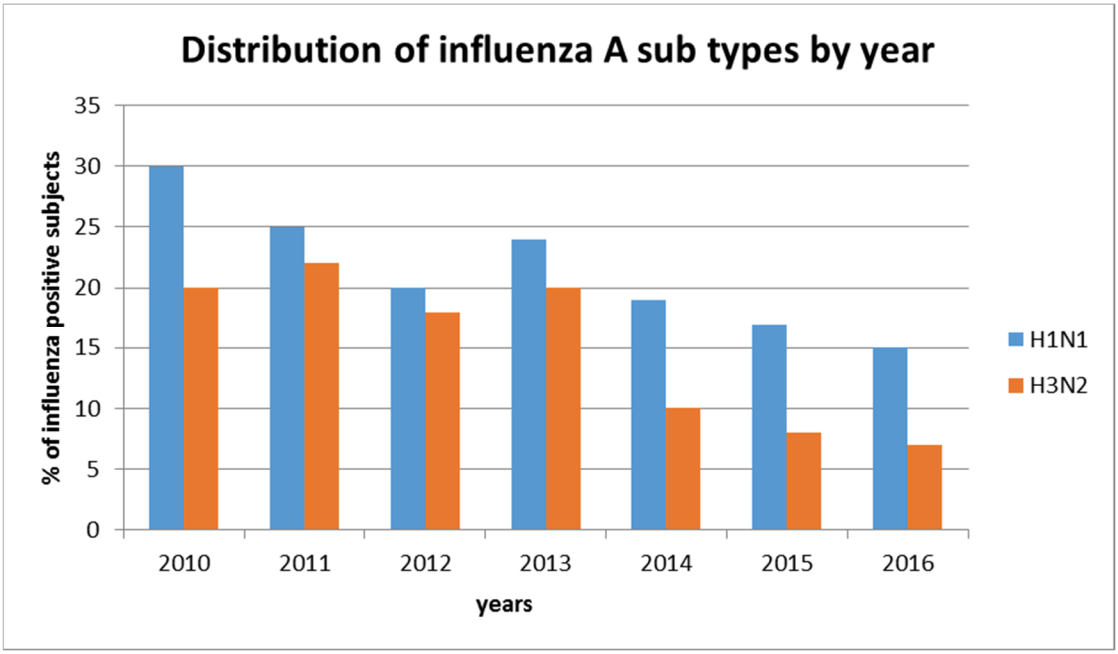


Figure 14 Distribution of Influenza A subtypes among all influenza cases by influenza season - <country> (Total cohort)

Refer to Figure 13

Template 21 Proportion of Influenza B lineage among all influenza cases by calendar year - <country> (Total cohort)

					95% CI	
Year	**Influenza B lineage**	**n**	**N**	**%**	**LL**	**UL**
2010	Victoria					
	Yamagata					
2011	Victoria					
	Yamagata					
2012	Victoria					
	Yamagata					
2013	Victoria					
	Yamagata					
2014	Victoria					
	Yamagata					
2015	Victoria					
	Yamagata					
2016	Victoria					
	Yamagata					
Total	Victoria					
	Yamagata					

N = Number of Influenza positive specimens with available test results by year
n = Number of positive specimens in a given category
% = n/N * 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Template 22 Proportion of Influenza B lineage among all influenza cases by influenza season - <country> (Total cohort)

					95% CI	
<Southern/northern hemisphere influenza season>	**Influenza B lineage**	**n**	**N**	**%**	**LL**	**UL**
May– Oct 2010	Victoria					
	Yamagata					
May– Oct 2011	Victoria					
	Yamagata					
May– Oct 2012	Victoria					
	Yamagata					
May– Oct 2013	Victoria					
	Yamagata					
May– Oct 2014	Victoria					
	Yamagata					
May– Oct 2015	Victoria					
	Yamagata					
May– Oct 2016	Victoria					
	Yamagata					
Total	Victoria					
	Yamagata					

N = Number of Influenza positive specimens with available test results by year
n = Number of positive specimens in a given category
% = n/N * 100
95%CI= exact confidence interval; LL=lower limit; UL=upper limit

Figure 15 Distribution of Influenza B lineage among all influenza cases by calendar year - <country> (Total cohort)

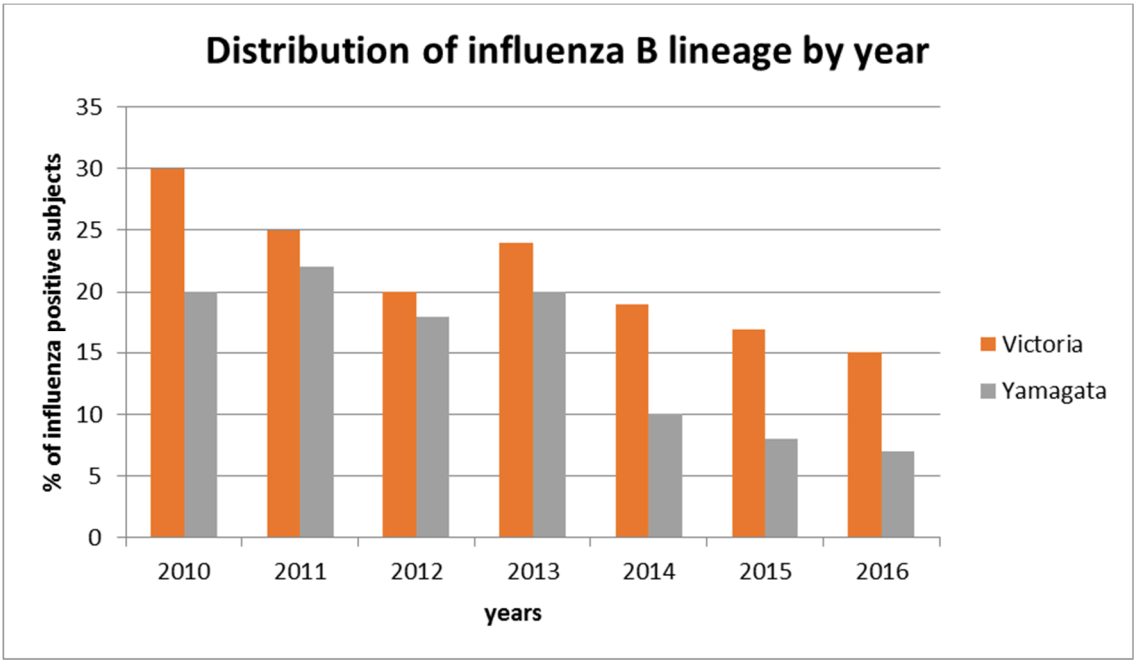


Figure 16 Distribution of Influenza B lineage among all influenza cases by influenza season - <country> (Total cohort)

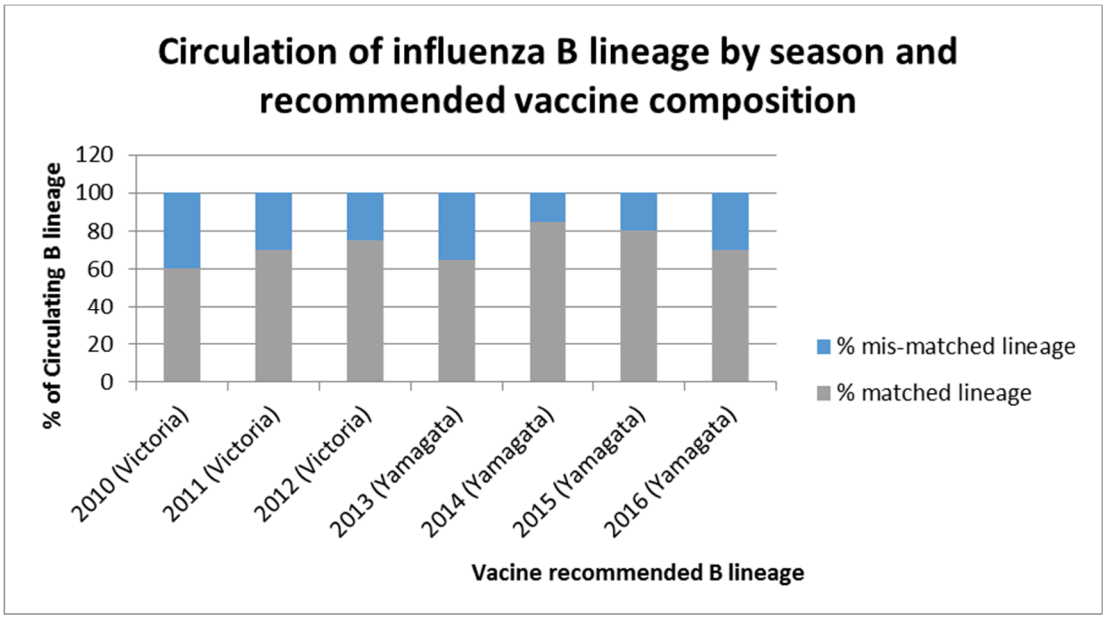
Refer to Figure 15

Template 23 Comparison of influenza B virus vaccine lineage and circulating lineage in the population by influenza season - <country> (Total cohort)

<Southern/northern hemisphere influenza season>	Circulating Influenza B lineages			Vaccine Recommendation*	% Match	% Mismatch
	B lineage	n	%			
2010	Victoria			Victoria		
	Yamagata			Victoria		
2011	Victoria			Victoria		
	Yamagata			Victoria		
2012	Victoria			Victoria		
	Yamagata			Victoria		
2013				Yamagata		
2014				Yamagata		
2015						
2016						

*http://www.who.int/influenza/vaccines/virus/recommendations/en/
n = Number of influenza positive specimens in a given category
% = n / Number of specimens with available results x 100
% Mismatch = 100% − % Circulating B lineage match with vaccine

Figure 17 Circulation of influenza B lineage by season and recommended vaccine composition - <country> (Total cohort)



Template 24 Summary of signs and symptoms by influenza types and influenza season - <country> (Total cohort)

			Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
<Southern/northern hemisphere influenza season>	**Signs and symptoms**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
May– Oct 2010	Sudden onset of symptoms	Yes						
		No						
		Unknown		-		-		
	Fever	Yes						
		No						
		Unknown		-		-		-
	Malice	Yes						
		No						
		Unknown		-		-		-
	Cough	Yes						
		No						
		Unknown		-		-		-
	Rhinorrhea	Yes						
		No						
		Unknown						
	Headache	Yes						
		No						
		Unknown		-		-		-
	Polypnea	Yes						
		No						
		Unknown		-		-		-

			Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
	Dyspnea	Yes						
		No						
		Unknown		-		-		-
	Vomiting	Yes						
		No						
		Unknown		-		-		-
	Myalgia	Yes						
		No						
		Unknown		-		-		-
	Arthralgia	Yes						
		No						
		Unknown		-		-		-
	Irritability	Yes						
		No						
		Unknown		-		-		-
	Odynophagia	Yes						
		No						
		Unknown		-		-		-
	Abdominal pain	Yes						
		No						
		Unknown		-		-		-
	Diarrhea	Yes						
		No						
		Unknown		-		-		-
	Conjunctivitis	Yes						
		No						
		Unknown		-		-		-
	Chest pain	Yes						
		No						
		Unknown		-		-		-
	Cyanosis	Yes						
		No						
		Unknown		-		-		-
	Chills	Yes						
		No						
		Unknown		-		-		-
May– Oct 2011								
May– Oct 2012								
…								
…								
Total								

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of subjects with available results x 100

Template 25 Summary of signs and symptoms by influenza A subtypes and B lineage and influenza season - <country> (Total cohort)

			Influenza A subtypes				Influenza B lineage			
			H1N1 N=XX		H3N2 N=XX		Victoria N=XX		Yamagata N=XX	
<Southern/northern hemisphere influenza season>	Signs and symptoms	Categories	n	%	n	%	n	%	n	%
May– Oct 2010	Sudden onset of symptoms	Yes								
		No								
		Unknown						-		-
	Fever	Yes								
		No								
		Unknown						-		-
	Malice	Yes								
		No								
		Unknown						-		-
	Cough	Yes								
		No								
		Unknown						-		-
	Rhinorrhea	Yes								
		No								
		Unknown								
	Headache	Yes								
		No								
		Unknown						-		-
	Polypnea	Yes								
		No								
		Unknown						-		-
	Dyspnea	Yes								
		No								
		Unknown						-		-
	Vomiting	Yes								
		No								
		Unknown						-		-
	Myalgia	Yes								
		No								
		Unknown						-		-
	Arthralgia	Yes								
		No								
		Unknown						-		-
	Irritability	Yes								
		No								
		Unknown						-		-

			Influenza A subtypes				Influenza B lineage			
			H1N1 N=XX		H3N2 N=XX		Victoria N=XX		Yamagata N=XX	
	Odynophagia	Yes								
		No								
		Unknown						-		-
	Abdominal pain	Yes								
		No								
		Unknown						-		-
	Diarrhea	Yes								
		No								
		Unknown						-		-
	Conjunctivitis	Yes								
		No								
		Unknown						-		-
	Chest pain	Yes								
		No								
		Unknown						-		-
	Cyanosis	Yes								
		No								
		Unknown						-		-
	Chills	Yes								
		No								
		Unknown						-		-
May– Oct 2011										
May– Oct 2012										
…										
…										
Total										

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 26 Summary of co-morbidity conditions by influenza types and influenza season- <country> (Total cohort)

			Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
<Southern/northern hemisphere influenza season>	**Co-morbidity condition**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
May– Oct 2010	Diabetes	Yes						
		No						
		Unknown		-		-		-
	Chronic obstructive pulmonary disease (COPD)	Yes						
		No						
		Unknown		-		-		-
	Asthma	Yes						
		No						
		Unknown		-		-		-

			Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
<Southern/northern hemisphere influenza season>	**Co-morbidity condition**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
	Inmunosuppression	Yes						
		No						
		Unknown		-		-		-
	Hypertension	Yes						
		No						
		Unknown		-		-		-
	HIV/AIDS	Yes						
		No						
		Unknown		-		-		-
	Cardiovascular disease	Yes						
		No						
		Unknown		-		-		-
	Obesity	Yes						
		No						
		Unknown		-		-		-
	Smoking	Yes						
		No						
		Unknown		-		-		-
	Chronic renal failure	Yes						
		No						
		Unknown		-		-		-
	Pregnancy	Yes						
		No						
		Unknown		-		-		-
	Months of pregnancy	n		-		-		-
		Mean		-		-		-
		SD		-		-		-
		Median		-		-		-
		Minimum		-		-		-
		Maximum		-		-		-
		N.A./Unknown		-		-		-
May– Oct 2011								
…								
….								
Total								

N = number of influenza positive specimens by groups
n = number of influenza positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 27 Summary of co-morbidity conditions by influenza A subtypes and B lineage and influenza season- <country> (Total cohort)

			Influenza A subtypes				Influenza B lineage		
			H1N1 N=XX		H3N2 N=XX		Victoria N=XX		Yamagata N=XX
<Southern/northern hemisphere influenza season>	**Co-morbidity condition**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	
May– Oct 2010	Diabetes	Yes							
		No							
		Unknown		-		-		-	
	Chronic obstructive pulmonary disease (COPD)	Yes							
		No							
		Unknown		-		-		-	
	Asthma	Yes							
		No							
		Unknown		-		-		-	
	Inmunosuppression	Yes							
		No							
		Unknown		-		-		-	
	Hypertension	Yes							
		No							
		Unknown		-		-		-	
	HIV/AIDS	Yes							
		No							
		Unknown		-		-		-	
	Cardiovascular disease	Yes							
		No							
		Unknown		-		-		-	
	Obesity	Yes							
		No							
		Unknown		-		-		-	
	Smoking	Yes							
		No							
		Unknown		-		-		-	
	Chronic renal failure	Yes							
		No							
		Unknown		-		-		-	
	Pregnancy	Yes							
		No							
		Unknown		-		-		-	
	Months of pregnancy	n		-		-		-	
		Mean		-		-		-	
		SD		-		-		-	
		Median		-		-		-	
		Minimum		-		-		-	
		Maximum		-		-		-	
		N.A./Unknown		-		-		-	
May– Oct 2011									
…									
Total									

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 28 Summary of treatments by influenza types and influenza season- <country> (Total cohort)

			Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
<Southern/northern hemisphere influenza season>	**Treatment**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
May– Oct 2010	Treatment received from the beginning of symptoms	Yes						
		No						
		Unknown		-		-		-
	Antivirals treatment	Yes						
		No						
		Unknown/NA		-		-		-
	Microbial Treatment	Yes						
		No						
		Unknown/NA		-		-		-
May– Oct 2011								
…								
Total								

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 29 Summary of treatments by influenza A subtypes and B lineage and influenza season - <country> (Total cohort)

			Influenza A subtypes				Influenza B lineage	
			H1N1 N=XX		H3N2 N=XX		Victoria N=XX	Yamagata N=XX
<Southern/northern hemisphere influenza season>	**Treatment**	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
May– Oct 2010	Treatment received from the beginning of symptoms	Yes						
		No						
		Unknown		-		-		
	Antivirals treatment	Yes						
		No						
		Unknown/NA		-		-		
	Microbial Treatment	Yes						
		No						
		Unknown/NA		-		-		
May– Oct 2011								
…								
Total								

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 30 Summary of outcome by influenza types and influenza season-<country> (Total cohort)

		Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
<Southern/northern hemisphere influenza season>	**Outcome**	**n**	**%**	**n**	**%**	**n**	**%**
May– Oct 2010	Discharged						
	Serious case						
	No serious case						
	Death						
	Missing		-		-		-
May– Oct 2011							
…							
Total							

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 31 Summary of outcome by influenza A subtypes and B lineage - <country> (Total cohort)

		Influenza A subtypes				Influenza B lineage			
		H1N1 N=XX		H3N2 N=XX		Victoria N=XX		Yamagata N=XX	
<Southern/northern hemisphere influenza season>	**Outcome**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
May– Oct 2010	Discharged								
	Serious case								
	No serious case								
	Death								
	Missing		-		-				-
May– Oct 2011									
…									
Total									

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 32 Summary of background information by influenza types - <country> (Total cohort)

		Influenza A positive N=XX		Influenza B positive N=XX		Influenza virus positive N = XX	
History	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**
Previous contact with other influenza cases	Yes						
	No						
	Missing		-		-		-
Previous contact with Birds	Yes						
	No						
	Missing		-		-		-
Previous contact with Pigs	Yes						
	No						
	Missing		-		-		-
Previous contact with other animals	Yes						
	No						
	Missing		-		-		-
Previous vaccination against seasonal influenza	Yes						
	No						
	Missing		-		-		-

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100

Template 33 Summary of background information by influenza A subtypes and B lineage - <country> (Total cohort)

		Influenza A subtypes				Influenza B lineage			
		H1N1 N=XX		H3N2 N=XX		Victoria N=XX		Yamagata N=XX	
History	**Categories**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Previous contact with other influenza cases	Yes								
	No								
	Missing		-		-				
Previous contact with Birds	Yes								
	No								
	Missing		-		-				
Previous contact with Pigs	Yes								
	No								
	Missing		-		-				
Previous contact with other animals	Yes								
	No								
	Missing		-		-				
Previous vaccination against seasonal influenza	Yes								
	No								
	Missing		-		-				

N = number of influenza positive specimens by groups
n = number of positive specimens in a given category
% = n / Number of specimens with available results x 100