Supporting Information

Using seroprevalence and immunisation coverage data to estimate the global burden of Congenital Rubella Syndrome, 1996-2010

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A: Analyses of the serological data collected before the introduction of RCV

1.1 Unpublished datasets used in the analyses

Table A: Numbers of females who were tested and positive for rubella antibodies in urban and rural areas in the study in Vellore, South India, 1999-2000 (Brown, Cutts, Samuel, Joseph, unpublished)[1].

	Rural		Urban	
Age (years)	**Number tested**	**Number positive**	**Number tested**	**Number positive**
1	29	1	41	6
2	38	4	33	14
3	41	8	36	15
4	45	8	47	20
5	30	6	40	16
6	44	8	42	24
7	40	19	35	25
8	52	36	41	30
9	49	26	34	25
10	52	38	44	40
11	56	53	36	27
12	48	39	45	42
13	48	37	46	37
14	50	38	38	37
15	38	30	23	20
16	53	45	46	45
17	53	46	40	38
18	64	57	50	45
19	50	45	36	34
20	50	48	38	33
21	42	37	31	28
22	46	38	46	44
23	38	36	30	29
24	38	34	34	33
25	68	59	48	46
26	39	37	43	42
27	49	47	25	23
28	40	36	42	42
29	33	30	30	30
30	62	58	55	53
31	29	26	16	16
32	34	31	26	26
33	28	25	25	25
34	35	32	12	12
35	63	60	38	36
36	23	23	26	25
37	26	23	21	18
38	40	38	49	46
39	30	29	21	21

Table B: Numbers of females who were tested and positive for rubella antibodies in the study in Kilifi, Kenya 1996-9 (Shulman et al, unpublished)[2-3]

Age group (years)	Number tested	Number positive
14-19	57	37
20-24	106	78
25-29	67	53
30-34	28	24
35-43	18	15

1.2 Rubella immunity testing

Rubella antibody screening for immunity has been widely used for 40 years. The test used has been refined over time. Initially screening was based on Haemagglutination Inhibition tests (HAI) and single Radical haemolysis (SRH) using a cut-off of 15 IU/ml, established to balance sensitivity of these tests against specificity (presence of low titre non-specific inhibition). Testing technology gradually changed to Enzyme-linked immunosorbent assay (EIA) through the 1980's – 90's initially using a cut-off of 10IU/ml and more recently to any detectible antibody level (4iu/ml). In parallel to these developments there has been a reduction in population antibody levels following widespread introduction of vaccine, which has been compensated for by improved sensitivity of assay.

1.3 Equations for the proportion susceptible

For people in the age range a_j-a_k, denoted by the short-hand notation $A_{j,k}$, the proportion susceptible in the catalytic model was given by the following equation:

$$s(A_{j,k}) = \begin{cases} \dfrac{e^{-\bar{\lambda}_y(a_j-0.5)} - e^{-\bar{\lambda}_y(a_k-0.5)}}{\bar{\lambda}_y(a_k-a_j)} & a_j, a_k < 13 years \\ \dfrac{(13-a_j)s(A_{j,13}) + (a_k-13)s(A_{13,k})}{a_k-a_j} & a_j < 13 years, a_k \geq 13 years \\ \dfrac{e^{-12\bar{\lambda}_y}(e^{-\bar{\lambda}_o(a_j-13)} - e^{-\bar{\lambda}_o(a_k-13)})}{\bar{\lambda}_o(a_k-a_j)} & a_j, a_k \geq 13 years \end{cases}$$

The numerator in the first and last equation equals the difference in the proportion susceptible between the lower and upper ages in the age range of interest, and therefore the proportion newly

infected in this age range and the denominator equals the force of infection (the rate at which they are infected) at this age, multiplied by the difference time spent in this age range. The equations can be derived by integrating the following expressions for the age-specific proportion susceptible over the age range of interest:

$$s(a) = \begin{cases} e^{-\bar{\lambda}_y (a-0.5)} & a < 13 \, years \\ e^{-12.5\bar{\lambda}_y} e^{-\bar{\lambda}_o (a-13)} & a \geq 13 \, years \end{cases}$$

1.4 Fitting the seroprevalence data and calculating 95% CI

1.4.1 The loglikelihood deviance

The catalytic models were fitted using maximum likelihood by minimizing the following expression for the (binomial) loglikelihood deviance for each datasets comprising *D* datapoints:

$$-2\left\{\sum_{j=1}^{D} \mathrm{K_j} \ln(\hat{p}_j) + (N_j - \mathrm{K_j}) \ln(1-\hat{p}_j) - \mathrm{K_j} \ln(p_j) - (N_j - \mathrm{K_j}) \ln(1-p_j)\right\}$$

where

K_j is the number of individuals in the j^{th} age group in the dataset who were seropositive;

N_j is the number of individuals represented in the j^{th} age group who were tested;

p_j is the proportion of individuals in the j^{th} age group in the dataset who were seropositive;

$\hat{p}_j$ is the model prediction of the proportion of individuals in the j^{th} age group in the dataset who were seropositive, and equal to 1-proportion of people in the same age group who were seronegative (see SI 1.3 for the equations).

The age groups used were the ones provided in the corresponding publication describing the study.

1.4.2 Calculating 95% CI

95% confidence intervals (CI) for the force of infection and (where applicable) the sensitivity of the assay for each dataset and model were calculated using non-parametric bootstrap for binary data, based on 1000 bootstrap datasets, following Shkedy et al[4].

With this approach, a single bootstrap dataset B (B=1..1000) comprised K_j^B seropositive people in age group j among N_j people in this age group who were tested. K_j^B was obtained by first assigning the status “seropositive” or “seronegative” to each of the N_i people in age group j in the dataset and drawing N_j samples with replacement from this population. K_j^B then equalled the number of people in the N_j samples who were positive. The fitting was repeated for each of the bootstrap datasets and the 95% CI for the force of infection was calculated as the 95% range of the force of infection estimates obtained from the B=1..1000 bootstrap datasets.

B: Sources of the bootstrap datasets

Table C: Datasets used to set up bootstrap files for the WHO Regions. Note that these datasets had been accepted after performing the selection procedure described in the methods.

Region	Datasets
African (AFRO)	Benin, 1993[5]; Congo, <1991[6]; Cote d'Ivoire, 1975[7] & 1985-6[8]; Ethiopia, 1981[9] & 1994[10]; Gabon, 1985[11]; Ghana, 1997[12]; Kenya, 1996-9 (Kilifi)[2-3]; Madagascar, 1990-1995[13]; Mozambique, 2002[14]; Nigeria, <1978[15], <2002[16] & 2007-8[17]; Senegal, 1996-2001[18]; South Africa, 2003[19], Zambia, 1979-80[20],
American, excluding Caribbean (AMRO, excl Caribbean)	Argentina, 1967-8 (urban & rural)[21], & 1981 (Mar de Plata)[22]; Brazil, 1967-8[21], 1987[23] & 1996-8[24]; Canada, <1967[25]; Chile 1967-8 (Santiago & rural)[21]; Mexico, 1987-88[26] & 1989[27]; Panama 1967-8 (Panama City & rural)[21]; Peru, 1967-8 (Lima & rural)[21] & 2003[28]; Uruguay, 1967-7 (urban and rural)[21]; USA <1967 (Atlanta & Houston)[25].
Caribbean	Haiti, 2003[29], Jamaica, 1967-8 (Kingston & rural)[21], Trinidad 1966-7[30], 1967-8 (Port au Spain & rural)[21]
Eastern Mediterranean (EMRO)	Bahrain, 1981[31]; Iran, 1993-95[32]; Jordan, 1982-3[33]; Kuwait, <1978[34]; Lebanon, 1980-1[35]; Morocco, 1969-70[36]; Pakistan, <1997[37] & 1999-2004[38]; Saudi Arabia, 1989[39] & 1992-93[40], Tunisia, <1970[41]; Yemen, 1985[42] & 2002-03[43]
European (EURO)	Czech Republic, <1967[25]; Denmark, <1967[25] &1983[44]; East Germany, 1990[45]; England, <1967[25] & 1986-7[46]; Finland, 1979[47]; France, <1967[25]; Kyrgyzstan, 2001[48]; Romania, <1989[49]; Turkey, 1998[50], 2003-04[51] & 2005[52].
South East Asian (SEARO)	Bangladesh, 2004-5[53]; India, 1968 (urban & rural Delhi)[54], 1972-3 (Chandrigarh & Lucknow)[54], 1976 (Calcutta)[55], <1987 (Delhi)[56], <1990 (Delhi)[57], 1999-2000 (urban and rural Vellore)[1]; Nepal, 2008[58], Thailand, 1978[59]
Western Pacific, excluding China & Australia (WPRO, excluding China & Australia)	Fiji, <1973[60]; Japan, <1967 (Sapporo &Ohtsu)[25]; Malaysia, <1972[61]; Singapore, 1975-79[62], Taiwan, 1984[63] & 1984-6[64]; Central Vietnam, 2009-2010[65]

Table D: Datasets used to set up bootstrap files for the Global Burden of Disease (GBD) regions. Note that these datasets had been accepted after performing the selection procedure described in the methods.

GBD Region	Setting from which dataset(s) were collected
Sub-Saharan Africa, Central	Congo, <1991[6]; Gabon, 1985[11]
Sub-Saharan Africa, East	Ethiopia, 1981[9] & 1994[10]; Kenya (Kilifi), 1996-9[2-3]; Madagascar, 1990-1995[13]; Mozambique, 2002[14]; Zambia, 1979-80[20]
Sub-Saharan Africa, Southern	South Africa, 2003[19]
Sub-Saharan Africa, West	Benin, 1993[5]; Cote d'Ivoire, 1975[7] & 1985-6[8]; Ghana, 1997[12]; Nigeria, <1978[15], <2002[16] & 2007-8[17]; Senegal, 1996-2001[18]
Caribbean	Haiti, 2003[29], Jamaica, 1967-8 (Kingston & rural)[21], Trinidad 1966-7[30], 1967-8 (Port au Spain & rural)[21]
Latin America, Andean	Peru, 1967-8 (Lima & rural)[21] & 2003[28]
Latin America, Central	Mexico, 1987-88[26] & 1989[27], Panama 1967-8 (Panama City & rural)[21]
Latin America, Southern	Argentina, 1967-8 (urban & rural)[21], & 1981 (Mar de Plata)[22], Chile (Santiago & rural), 1967-8[21]; Uruguay, 1967-7 (urban and rural)[21]
Latin America, Tropical	Brazil, 1967-8[21], 1987[23] & 1996-8[24]
North America, High Income	Canada, <1967[25], USA <1967 (Atlanta & Houston)[25]
Asia Central	Kyrgyzstan, 2001[48]
North Africa / Middle East	Bahrain, 1981[31]; Iran, 1993-95[32]; Jordan, 1982-3[33]; Kuwait, <1978[34]; Lebanon, 1980-81[35]; Morocco, 1969-1970[36]; Saudi Arabia, 1989[39] & 1992-93[40] Tunisia, <1970[41]; Turkey, 1998[66], 2003-4[51] & 2005[52]; Yemen, 1985[42] & 2002-03[43]
Europe, Eastern	Taken to be identical to those for Europe Central (Romania, <1989[49]; Czech Republic, <1967[25]), as no datasets were available from the countries in this grouping
Europe Central	Romania, <1989[49]; Czech Republic, <1967[25]
Europe, Western	Denmark, <1967[25] &1983[44]; England, 1986-87[46] & <1967[25]; East Germany, 1990[45]; Finland, 1979[47]; France, <1967[25].
Asia East	China, 1979-80[67]; Taiwan, 1984[63] & 1984-6[64]
Asia, South	Bangladesh 2004-5[53]; India, 1968 (urban & rural Delhi)[54], 1972-3 (Chandrigarh & Lucknow)[54], 1976 (Calcutta)[55], <1987 (Delhi)[56], <1990 (Delhi)[57], 1999-2000 (urban & rural Vellore)[1]; Nepal, 2008[58], Pakistan, <1997[37] & 1999-2004[38]
Asia Pacific, High Income	Japan, <1967 (Ohtsu & Sapporo)[25]; Singapore, 1975-9[62]
Asia, Southeast	Malaysia, <1972[61]; Thailand, 1978[59]; Central Vietnam, 2009-2010[65]
Australasia	Australia, <1967[25]
Oceania	Fiji, <1973[60]

Table E: Summary of the bootstrap datasets used to estimate the CRS incidence for each country using catalytic models (countries which had not introduced RCV by 2010) or the transmission model (countries which had introduced RCV by 2010), using either the WHO regional or GBD grouping to assign datasets for countries without serological datasets from before the introduction of RCV. See Table C and Table D for the datasets used to make up the bootstrap datasets. See Table H and Table I for estimates of the prevaccination force of infection and CRS incidence. Countries which had not introduced RCV by 2010 are shaded in grey.

Country	**Bootstrap dataset used:**	
	WHO regional grouping	**GBD grouping**
Africa		
Algeria	AFRO region	North Africa, Middle East
Angola	AFRO region	Sub-Saharan Africa, Central
Benin	Benin, 1993[5]	Benin, 1993[5]
Botswana	AFRO region	Sub-Saharan Africa, Southern
Burkina Faso	AFRO region	Sub-Saharan Africa, West
Burundi	AFRO region	Sub-Saharan Africa, East
Cameroon	AFRO region	Sub-Saharan Africa, West
Cape Verde	AFRO region	Sub-Saharan Africa, West
Central African Republic	AFRO region	Sub-Saharan Africa, Central
Chad	AFRO region	Sub-Saharan Africa, West
Comoros	AFRO region	Sub-Saharan Africa, East
Congo	AFRO region	Sub-Saharan Africa, Central
Côte d'Ivoire	Cote d'Ivoire, 1975[7] & 1985-6[8]	Cote d'Ivoire, 1975[7] & 1985-6[8]
Democratic Republic of the Congo	AFRO region	Sub-Saharan Africa, Central
Equatorial Guinea	AFRO region	Sub-Saharan Africa, Central
Eritrea	AFRO region	Sub-Saharan Africa, East
Ethiopia	Ethiopia, 1981[9] & 1994[10]	Ethiopia, 1981[9] & 1994[10]
Gabon	Gabon, 1985[11]	Gabon, 1985[11]
Gambia	AFRO region	Sub-Saharan Africa, West
Ghana	Ghana, 1997[12]	Ghana, 1997[12]
Guinea	AFRO region	Sub-Saharan Africa, West
Guinea-Bissau	AFRO region	Sub-Saharan Africa, West
Kenya	Kenya (Kilifi), 1996-9[2-3]	Kenya (Kilifi), 1996-9[2-3]
Lesotho	AFRO region	Sub-Saharan Africa, Southern
Liberia	AFRO region	Sub-Saharan Africa, West
Madagascar	Madagascar, 1990-1995 [13]	Madagascar, 1990-1995 [13]
Malawi	AFRO region	Sub-Saharan Africa, East
Mali	AFRO region	Sub-Saharan Africa, West
Mauritania	AFRO region	Sub-Saharan Africa, West
Mauritius	AFRO region	Asia, South East
Mozambique	Mozambique, 2002[14]	Mozambique, 2002[14]
Namibia	AFRO region	Sub-Saharan Africa, Southern
Niger	AFRO region	Sub-Saharan Africa, West
Nigeria	AFRO region	Sub-Saharan Africa, West
Réunion	AFRO region	Asia, South East
Rwanda	AFRO region	Sub-Saharan Africa, East
Sao Tome and Principe	AFRO region	Sub-Saharan Africa, West
Senegal	Senegal, 1996-2001 [18]	Senegal, 1996-2001 [18]

Country	Bootstrap dataset used:	
	WHO regional grouping	**GBD grouping**
Sierra Leone	AFRO region	Sub-Saharan Africa, West
South Africa	South Africa, 2003 [19]	South Africa, 2003 [19]
Swaziland	AFRO region	Sub-Saharan Africa, Southern
Togo	AFRO region	Sub-Saharan Africa, West
Uganda	AFRO region	Sub-Saharan Africa, East
United Republic of Tanzania	AFRO region	Sub-Saharan Africa, East
Western Sahara	AFRO region	North Africa, Middle East
Zambia	Zambia, 1979-80 [20]	Zambia, 1979-80 [20]
Zimbabwe	AFRO region	Sub-Saharan Africa, Southern
Americas		
Argentina	Argentina, 1967-8 (urban & rural)[21], & 1981 (Mar de Plata)[22]	Argentina, 1967-8 (urban & rural)[21], & 1981 (Mar de Plata)[22]
Aruba	Caribbean	Caribbean
Bahamas	Caribbean	Caribbean
Barbados	Caribbean	Caribbean
Belize	Caribbean	Caribbean
Bolivia	AMRO region, excluding the Caribbean	Latin America, Andean
Brazil	Brazil, 1967-8[21], 1987[23] & 1996-8[24]	Brazil, 1967-8[21], 1987[23] & 1996-8[24]
Canada	Canada, <1967[25]	Canada, <1967[25]
Chile	Chile 1967-8 (Santiago & rural)[21]	Chile 1967-8 (Santiago & rural)[21]
Colombia	AMRO region, excluding the Caribbean	Latin America, Central
Costa Rica	AMRO region, excluding the Caribbean	Latin America, Central
Cuba	Caribbean	Caribbean
Dominican Republic	Caribbean	Caribbean
Ecuador	AMRO region, excluding the Caribbean	Latin America, Andean
El Salvador	AMRO region, excluding the Caribbean	Latin America, Central
French Guiana	Caribbean	Caribbean
Grenada	Caribbean	Caribbean
Guadeloupe	Caribbean	Caribbean
Guatemala	AMRO region, excluding the Caribbean	Latin America, Central
Guyana	Caribbean	Caribbean
Haiti	Haiti, 2003[29]	Haiti, 2003[29]
Honduras	AMRO region, excluding the Caribbean	Latin America, Central
Jamaica	Jamaica, 1967-8 (Kingston & rural)[21]	Jamaica, 1967-8 (Kingston & rural)[21]
Martinique	Caribbean	Caribbean
Mexico	Mexico, 1987-88[26] & 1989[27]	Mexico, 1987-88[26] & 1989[27]
Netherlands Antilles	Caribbean	Caribbean
Nicaragua	AMRO region, excluding the	Latin America, Central

	Caribbean	
Country	**Bootstrap dataset used:**	
	WHO regional grouping	**GBD grouping**
Panama	Panama 1967-8 (Panama City & rural)[21]	Panama 1967-8 (Panama City & rural)[21]
Paraguay	AMRO region, excluding the Caribbean	Latin America, Tropical
Peru	Peru, 1967-8 (Lima & rural)[21] & 2003[28]	Peru, 1967-8 (Lima & rural)[21] & 2003[28]
Puerto Rico	USA (Atlanta and Houston), <1967[25]	USA (Atlanta and Houston), <1967[25]
Saint Lucia	Caribbean	Caribbean
Saint Vincent and the Grenadines	Caribbean	Caribbean
Suriname	Caribbean	Caribbean
Trinidad and Tobago	Trinidad 1966-7[30], 1967-8 (Port au Spain & rural)[21]	Trinidad 1966-7[30], 1967-8 (Port au Spain & rural)[21]
USA	USA <1967 (Atlanta & Houston)[25]	USA <1967 (Atlanta & Houston)[25]
US Virgin Islands	USA <1967 (Atlanta & Houston)[25]	USA <1967 (Atlanta & Houston)[25]
Uruguay	Uruguay, 1967-7 (urban and rural)[21]	Uruguay, 1967-7 (urban and rural)[21]
Venezuela	AMRO region, excluding the Caribbean	Latin America, Central
Eastern Mediterranean		
Afghanistan	EMRO region	Asia, South
Bahrain	Bahrain, 1981[31]	Bahrain, 1981[31]
Djibouti	EMRO region	Sub-Saharan Africa, East
Egypt	EMRO region	North Africa / Middle East
Iran	Iran, 1993-95[32]	Iran, 1993-95[32]
Iraq	EMRO region	North Africa / Middle East
Jordan	Jordan, 1982-3[33]	Jordan, 1982-3[33]
Kuwait	Kuwait, <1978[34]	Kuwait, <1978[34]
Lebanon	Lebanon, 1980-81[35]	Lebanon, 1980-81[35]
Libya	EMRO region	North Africa / Middle East
Morocco	Morocco, 1969-1970[36]	Morocco, 1969-1970[36]
Oman	EMRO region	North Africa / Middle East
Pakistan	Pakistan, <1997[37] & 1999-2004[38]	Pakistan, <1997[37] & 1999-2004[38]
Qatar	EMRO region	North Africa / Middle East
Saudi Arabia	Saudi Arabia, 1989[39] & 1992-3[40]	Saudi Arabia, 1989[39] & 1992-3[40]
Somalia	EMRO region	Sub-Saharan Africa, East
Sudan	EMRO region	Sub-Saharan Africa, East
Syrian Arab Republic	EMRO region	North Africa/ Middle East
Tunisia	Tunisia, <1970[41]	Tunisia, <1970[41]
United Arab Emirates	EMRO region	North Africa / Middle East
Yemen	Yemen, 1985[42] & 2002-3[43]	Yemen, 1985[42] & 2002-3[43]
Europe		
Albania	EURO region	Europe, Central
Armenia	EURO region	Asia, Central
Austria	EURO region	Europe, Western

Azerbaijan	EURO region	Asia, Central
Country	**Bootstrap dataset used:**	
	WHO regional grouping	**GBD grouping**
Belarus	EURO region	Europe, Eastern
Belgium	EURO region	Europe, Western
Bosnia and Herzegovina	EURO region	Europe, Central
Bulgaria	EURO region	Europe, Central
Channel Islands	EURO region	Europe, Western
Croatia	EURO region	Europe, Central
Cyprus	EURO region	Europe, Western
Czech Republic	Czech Republic, <1967[25]	Czech Republic, <1967[25]
Denmark	Denmark, <1967[25] &1983[44]	Denmark, <1967[25] &1983[44]
Estonia	EURO region	Europe, Eastern
Finland	Finland, 1979[47]	Finland, 1979[47]
France	France, <1967[25]	France, <1967[25]
Georgia	EURO region	Asia, Central
Germany	East Germany, 1990[45]	East Germany, 1990[45]
Greece	EURO region	Europe, Western
Hungary	EURO region	Europe, Central
Iceland	EURO region	Europe, Western
Ireland	EURO region	Europe, Western
Israel	EURO region	Europe, Western
Italy	EURO region	Europe, Western
Kazakhstan	EURO region	Asia, Central
Kyrgyzstan	Kyrgyzstan, 2001[48]	Kyrgyzstan, 2001[48]
Latvia	EURO region	Europe, Eastern
Lithuania	EURO region	Europe, Eastern
Luxembourg	EURO region	Europe, Western
Malta	EURO region	Europe, Western
Montenegro	EURO region	Europe, Central
Netherlands	EURO region	Europe, Western
Norway	EURO region	Europe, Western
Poland	EURO region	Europe, Central
Portugal	EURO region	Europe, Western
Moldova	EURO region	Europe, Eastern
Romania	Romania, <1989[49]	Romania, <1989[49]
Russia	EURO region	Europe, Eastern
Serbia	EURO region	Europe, Central
Slovakia	EURO region	Europe, Central
Slovenia	EURO region	Europe, Central
Spain	EURO region	Europe, Western
Sweden	EURO region	Europe, Western
Switzerland	EURO region	Europe, Western
Macedonia	EURO region	Europe, Central
Tajikistan	EURO region	Asia, Central
Turkey	Turkey, 1998[50], 2003-04[51] & 2005[52]	Turkey, 1998[50], 2003-04[51] & 2005[52]
Turkmenistan	EURO region	Asia, Central
Ukraine	EURO region	Europe, Eastern
United Kingdom	England, <1967[25] & 1986-87[46]	England, <1967[25] & 1986-87[46]
Uzbekistan	EURO region	Asia, Central

Country	Bootstrap dataset used:	
	WHO regional grouping	**GBD grouping**
South East Asia		
Bangladesh	Bangladesh, 2004-5[53]	Bangladesh, 2004-5[53]
Bhutan	SEARO region	Asia, South
India	India, 1968 (urban & rural Delhi)[54], 1972-3 (Chandrigarh & Lucknow)[54], 1976 (Calcutta)[55], <1987 (Delhi)[56], <1990 (Delhi)[57], 1999-2000 (urban and rural Vellore)[1]	India, 1968 (urban & rural Delhi)[54], 1972-3 (Chandrigarh & Lucknow)[54], 1976 (Calcutta)[55], <1987 (Delhi)[56], <1990 (Delhi)[57], 1999-2000 (urban and rural Vellore)[1]
Indonesia	SEARO region	Asia, Southeast
Maldives	SEARO region	Asia, Southeast
Myanmar	SEARO region	Asia, Southeast
Nepal	Nepal, 2008[58]	Nepal, 2008[58]
Sri Lanka	SEARO region	Asia, Southeast
Thailand	Thailand, 1978[59]	Thailand, 1978[59]
Timor-Leste	SEARO region	Asia, Southeast
Western Pacific		
Australia	Australia, <1967[25]	Australia, <1967[25]
Brunei Darussalam	WPRO region, excluding China & Australia	Asia Pacific, High Income
Cambodia	WPRO region, excluding China & Australia	Asia, South East
China	China, 1979-80[67]	China, 1979-80[67]
China (Hong Kong)	China, 1979-80[67]	China, 1979-80[67]
China (Macao)	China, 1979-80[67]	China, 1979-80[67]
Fiji	Fiji, <1973[60]	Fiji, <1973[60]
French Polynesia	WPRO region, excluding China & Australia	Oceania
Guam	WPRO region, excluding China & Australia	Oceania
Japan	Japan, <1967 (Sapporo &Ohtsu)[25]	Japan, <1967 (Sapporo &Ohtsu)[25]
Laos	WPRO region, excluding China & Australia	Asia, Southeast
Malaysia	Malaysia, <1972[61]	Malaysia, <1972[61]
Micronesia	WPRO region, excluding China & Australia	Oceania
Micronesia (Fed. States)	WPRO region, excluding China & Australia	Oceania
Mongolia	WPRO region, excluding China & Australia	Asia, Central
New Caledonia	WPRO region, excluding China & Australia	Oceania
New Zealand	Australia, <1967[25]	Australia, <1967[25]
Papua New Guinea	WPRO region, excluding China & Australia	Oceania
Philippines	WPRO region, excluding China & Australia	Asia, Southeast
Polynesia	WPRO region, excluding China & Australia	Oceania

Country	Bootstrap dataset used:	
	WHO regional grouping	**GBD grouping**
Republic of Korea	WPRO region, excluding China & Australia	Asia Pacific, high income
Samoa	WPRO region, excluding China & Australia	Oceania
Singapore	Singapore, 1975-9[62]	Singapore, 1975-9[62]
Solomon Islands	WPRO region, excluding China & Australia	Oceania
Tonga	WPRO region, excluding China & Australia	Oceania
Vanuatu	WPRO region, excluding China & Australia	Oceania
Vietnam	Central Vietnam, 2009-2010[65]	Central Vietnam, 2009-2010[65]

C: Description of the transmission model

3.1 Model structure

Figure A summarises the general structure of the model. The population is stratified into those who have maternal immunity, those who are susceptible, pre-infectious (infected but not yet infectious), infectious and immune. The demography in the model was described using a realistic age structured (RAS) population[68], with individuals stratified by sex and into 75 age strata, corresponding to the ages <1, 1-<2, 2-<3, …, 74-<75 years.

Single year age strata were used in preference to strata involving a wide age range, in order to avoid introducing inaccuracies when ageing the population from one age group into the next. For example, if the population were to be merged into compartments comprising 5 year age groups, we would need to apply an ageing rate to each group in order to move the population from one age group to the next. This is not ideal since we would be applying the ageing rate to those who had just moved into the compartment. This could result in some of those aged 30 years, for example, entering the 35-39 year old compartment within days of them becoming 30 years old. To increase consistency with the age grouping available for the mortality rates and therefore the age distribution in the population, we have considered all those aged over 75 years, as opposed to those aged over 70 years, as a single group.

For countries with a population growth rate of <2%/year, the age structure was assumed to be rectangular, with a constant birth rate over time, 10000 people in each single year age category and with individuals surviving until age 75 years before dying. For growing populations (growth rate >2%/year), we used the country-and age-specific mortality rate, calculated from survival data for the period 2005-2010 from UN population databases.[69] Therefore, the number of people of age *a* at a given time *t* $N_a(t)$ depends on the mortality rate. The number of births in the model was calculated by multiplying model predictions of the population size in the given year by the crude annual per capita birth rate for the period

2005-2010, obtained from UN population databases. Both the mortality and crude birth rates in the model were assumed to be fixed over time. Note that the absolute magnitude of the numbers of births in the model does not greatly influence the absolute numbers of CRS cases predicted for the global burden, since these were calculated by multiplying model predictions of the age-specific number of CRS cases per live birth by the observed numbers of live births by maternal age, as seen in UN population databases[69] and then summing the resulting numbers over all maternal ages.

Individuals are born into the first age stratum (stratum a=0) on the 31st August of each year and are assumed to have maternal immunity for 6 months. Although this approach for introducing newborns into the population may be less "natural" than allowing newborns to enter the first age stratum continuously over time, it facilitates tracking the exact time when individuals in the model are aged 6 months, when they lose maternal immunity and can first be vaccinated. Following standard approaches[68] individuals in each age stratum move to the subsequent age stratum on the 31st August of each year, at the same time as vaccination occurs (see below), and leave the model once they reach age 75 years.

The force of infection in the model at a given time t ($\lambda_y(t)$ and $\lambda_o(t)$) depends on age-specific contact between people and the prevalence of infectious people, with the contact parameters calculated from average annual force of infection estimates from seroprevalence data (see section 3.3).

For convenience, vaccination is implemented on a single day each year in the model, which is the simplest and least computationally intensive way of ensuring that the intended coverage is attained. For example, if we were to assume that vaccination campaigns are carried out over a period of a few weeks, we would need to keep track of how many individuals have been vaccinated in each time step in the model, and keep updating how many still need to be vaccinated in order to attain the required coverage. Estimates of the

overall burden of CRS obtained by introducing vaccination on a single day should be similar to that obtained by implementing vaccination with the same overall coverage over a period of weeks or months.

We note that an SEIR model could have also been used to calculate the CRS burden for countries which had not introduced RCV by 2010. However, doing so would have increased the computational burden but would not have affected the results. For example, the force of infection estimated using the catalytic model was used to calculate the contact parameters which were included in the transmission model and the latter, in turn, would have reproduced the same force of infection that was used to calculate the contact parameters in the transmission model.

We also note that the model does not include any effects of seasonality or metapopulation dynamics. Data on these effects are limited and including their effects would have increased the computational burden without affecting the results. For example, the overall effect of seasonality would be to increase the predicted CRS incidence in approximately one half of the year and decrease it in the other half of the year but the overall average annual CRS incidence, which is the value that of interest in these analyses, is unaffected. Likewise, including metapopulation dynamics, would result in increased estimates in some parts of each country, and decrease them elsewhere, with the overall estimates remaining similar.

Table F and Table G give definitions of the variables and parameters respectively that are used in the model. Throughout the description, we use the subscript "*y"* to refer to younger individuals (aged <13 years) and the subscript "*o"* to refer to older individuals (aged ≥13 years). Where necessary, the subscript "w" is used to denote females.

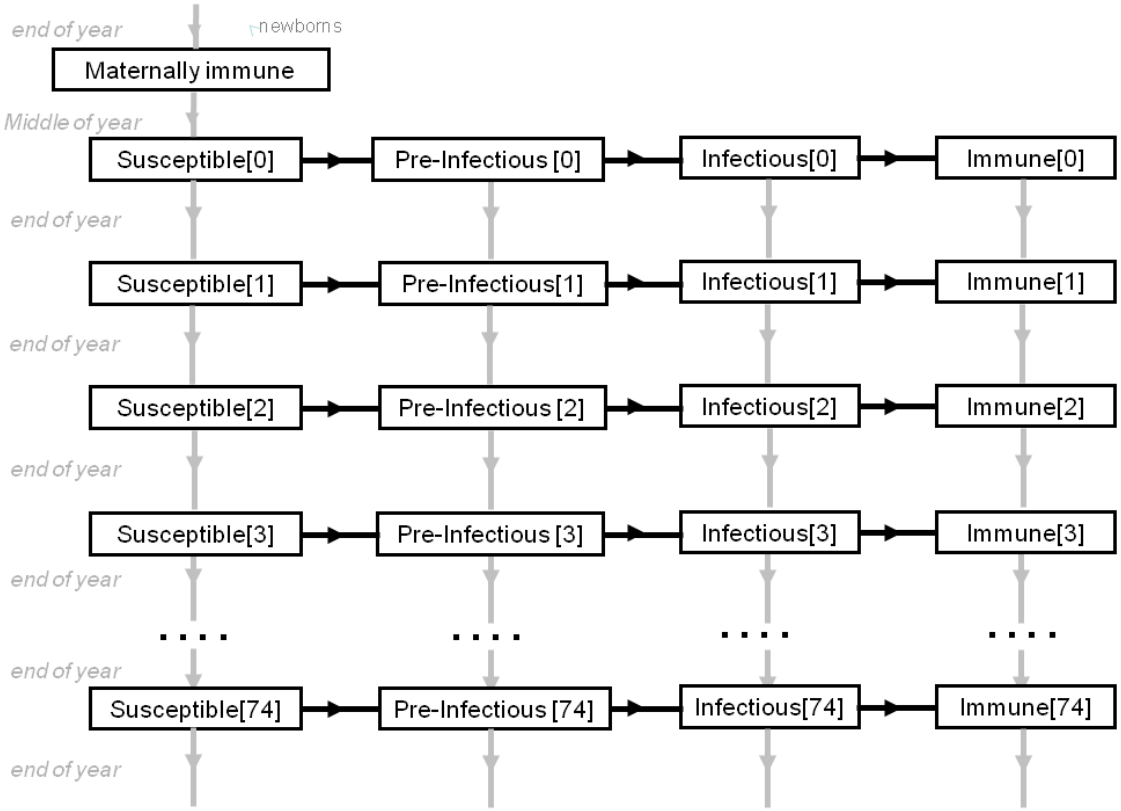

Figure A: General structure of the transmission model used to recreate the epidemiology of rubella, before the introduction of vaccination.

Table F**:** Summary of the definitions of compartments and variables used in the model. Where necessary in the equations, the subscript "w" is used to denote females.

Variable	Definition
$M_g(t)$	Number of individuals of gender *g* with maternal immunity at time *t*.
$S_{a,g}(t)$	Number of susceptible individuals of gender *g* aged *a* years at time *t.*
$E_{a,g}(t)$	Number of individuals in the pre-infectious category (infected but not infectious) of gender *g* and age *a* years at time *t.*
$I_{a,g}(t)$	Number of infectious individuals of gender *g* and aged *a* years at time *t.*
$I_y(t)$, $I_o(t)$	Number of younger and older infectious individuals at time *t.*
$\bar{I}_y$, $\bar{I}_0$	Average number of younger and older infectious individuals before the introduction of vaccination.
$R_{a,g}(t)$	Number of individuals of gender *g* and aged *a* years at time *t* who are immune either as a result of vaccination or natural infection.
$N_a(t)$	Total number of people (males and females combined) aged *a* at time *t*.
$N_y(t)$, $N_o(t)$	Total number of younger and older individuals at time *t* (aged <13 and ≥13 years respectively).

Table G**:** Summary of the definitions of the transition-related parameters used in the analyses

Parameter	Definition
$\lambda_a(t)$, $\lambda_y(t)$, $\lambda_o(t)$	The force of infection for individuals in a given age group at time *t*. The subscript *a* refers to individuals of age *a;* the subscripts *y* ('younger') and *o* ('older') refer to individuals aged <13 and ≥13 years respectively.
$\bar{\lambda}_y$, $\bar{\lambda}_0$	The average force of infection before the introduction of vaccination for individuals aged <13 years ('younger') and ≥13 years ('older'), respectively.
β_{yo}	The rate at which specific younger susceptible individuals come into effective contact with older infectious persons per unit time. An effective contact is defined as one which is sufficient to lead to transmission between an infectious and susceptible individual[70]. The definitions of β_{oy}, β_{oo}, β_{yy} are analogous.
c_{yo}	The number of younger susceptible individuals effectively contacted by each older infectious person per unit time. An effective contact is defined as one which is sufficient to lead to transmission between an infectious and susceptible individual[70]. The definitions of c_{oy}, c_{oo}, c_{yy} are analogous.
m_a	The mortality rate for individuals of age *a*. For populations which are assumed to be stable over time, the mortality rate is assumed to be zero until age 75 years, when all individuals leave the model. For growing countries, the rate is calculated using survival data for 2005-2010 from UN population databases[69].
$v_{a,g}(t)$	The proportion of individuals of age *a* of gender *g* who are vaccinated at time *t*. The coverage data are those estimated and/or reported to WHO and supplemented by the literature, where available.
$B_g(t)$	The number of live births each year for males or females in the model. Assumed to be 2500 per year for populations which are assumed to remain the same size over time. For countries in which the population is increasing over time, the numbers of live births was calculated as the product of the predicted population size and the crude per capita birth rate, obtained from UN population databases[69]. Note that the absolute magnitude of the numbers of births in the model does not greatly influence the absolute numbers of CRS cases predicted for the global burden, since these were calculated by multiplying model predictions of the age-specific number of CRS cases per live birth by the observed numbers of live births by maternal age, as seen in UN population databases[69] and then summing the resulting numbers over all maternal ages.
f	The rate at which individuals in the pre-infectious category become infectious, taken to equal 0.1/day, equivalent to assuming an average pre-infectious period of 10 days.
r	The rate at which infectious individuals recover and become immune, taken to equal 0.909 per day, equivalent to assuming an average infectious period of 11 days.
T_{crs}	Time period during which there is an increased risk of the child being born with CRS, if the mother is infected whilst pregnant.
T_E	Last year of the model simulations, 2010

3.2 Model equations

The equations used in the transmission model depend on whether the model described the transmission dynamics in a stable population with a rectangular age distribution or one in which the population size was assumed to increase over time. The differential equations

describing the transmission of rubella in growing populations in age stratum *a* (a=0, 1, 2, ...,74 years) are provided below (see Table F and Table G for the definitions of variables and parameters). The corresponding equations considering a population which is assumed to remain stable over time are identical, except that the mortality rate for all age strata ($m_a(t)$) is assumed to be zero until individuals reach age 75 years, when they leave the model.

$$\frac{dM_g(t)}{dt} = -m_0 M_g(t) \qquad 0 < t < 182 \bmod 365$$

$$\frac{dS_{a,g}(t)}{dt} = -\lambda_a(t) S_{a,g}(t) - m_a S_{a,g}(t)$$

$$\frac{dE_{a,g}(t)}{dt} = \lambda_a(t) S_{a,g}(t) - m_a E_{a,g}(t) - f E_{a,g}(t)$$

$$\frac{dI_{a,g}(t)}{dt} = f E_{a,g}(t) - m_a I_{a,g}(t) - r I_{a,g}(t)$$

$$\frac{dR_{a,g}(t)}{dt} = r I_{a,g}(t) - m_a R_{a,g}(t)$$

The equations for the transitions occurring on 31st August (denoted by *T*) each year are as follows:

$M_g(T) = B_g(T)$

$S_{a,g}(T) = S_{a-1,g}(T-\delta t)(1-v_{a,g}-m_{a-1}-\lambda_{a-1}(T-\delta t))$ *for 0< a <74* years

$E_{a,g}(T) = E_{a-1,g}(T-\delta t)(1-m_{a-1}-f)+\lambda_{a-1}(T-\delta t)S_{a-1,g}(T-\delta t)$ *for 0< a <74* years

$I_{a,g}(T) = I_{a-1,g}(T-\delta t)(1-m_{a-1}-r)+f\, E_{a-1,g}(T-\delta t)$ *for 0< a <74* years

$R_{a,g}(T) = R_{a-1,g}(T-\delta t)(1-m_{a-1}-r)+r I_{a-1,g}(T-\delta t)+ v_{a,g}\, S_{a-1,g}(T-\delta t)$ *for 0< a ≤75* years

The equations for the transitions occurring 6 months after the 31st August (or equivalently, 28th February), when individuals in the first year of life lose their maternal immunity are:

$S_{0,g}(T) = M_g(T-\delta t)(1-m_0-v_{0.5,g})$

$M_g(T) = 0$

The equations were solved using a specially written C-program, using the Euler method with a time step, δt, of 0.25 day. The Euler method was used in preference to the Runge-Kutta method to facilitate movement of each age stratum in the model into the next at the end of each year. For example, following the standard approach of Schenzle (1984)[68], individuals in each age stratum are moved into the next age stratum at the end of each year, which is straightforward to implement if the equations are solved using the Euler method. However it is not straightforward to implement using the Runge Kutta method, for which the average value over various steps (depending on the variant of the method used) is used when integrating the equations. Given the small time step used (0.25 days) predictions based on the Euler method will be very similar to those based on the Runge-Kutta method.

The model was run for 170 simulated years before the introduction of RCV, starting from the equilibrium numbers of individuals in each compartment, and with a population size of 750,000 ($N(T_0)$), with equal numbers of males and females.

The number of CRS cases per 100,000 live births occurring among mothers in age group $A_{j,k}$ (spanning the age groups a_j-a_k) at time t was calculated using the model prediction of the daily force of infection at time t using the following equation:

$$I_{CRS}(A_{j,k},t) = \frac{\sum_{a=a_j}^{a_k} S_{a,w}(t)(1-e^{-T_{CRS}\lambda_o(t)}) \times 0.65 \times 100000}{\sum_{a=a_j}^{a_k} N_{a,w}(t)}$$

The number of CRS cases per 100,000 live births in a given year occurring among mothers in a given age group was calculated by taking the average of the values in each time step in the year.

The equation can be derived by first assuming that both infection with rubella and the proportion of women at a given age that are susceptible are independent of whether or not a

woman is pregnant. The proportion of pregnant women in a given age group $A_{j,k}$ at a given time that are infected during the first 16 weeks of pregnancy is therefore the same as the proportion of women of that age that are susceptible ($\sum_{a=a_j}^{a_k} S_{a,w}(t) \Big/ \sum_{a=a_j}^{a_k} N_{a,w}(t)$) multiplied by the average risk of infection during a 16 week period $(1-e^{-T_{CRS}\lambda_0(t)})$. Multiplying the resulting expression by the risk that a child is born with CRS, if the mother is infected during the first 16 weeks of pregnancy (0.65), we obtain an estimate of the proportion of pregnant women of age *a* at time *t* whose pregnancies (or equivalently, live births) result in a child with CRS. Summing over all time steps in a year, we obtain the proportion of all pregnancies (or live births) at age *a* in that year that result in children born with CRS.

3.3 Contact parameters in the model

The contact parameters in the model were assumed to differ between younger and older individuals according to the following matrix of "Who Acquired Infection From Whom":

$$\begin{array}{c} \\ \leq 13yrs \\ > 13yrs \end{array} \begin{array}{c} \begin{array}{cc} \leq 13yrs & > 13yrs \end{array} \\ \begin{pmatrix} \beta_1 & 0.7\beta_2 \\ 0.7\beta_2 & \beta_2 \end{pmatrix} \end{array}$$

For this matrix, the rate at which those aged <13 years come into effective contact with others of the same age (β_1) differs from the rate at which older individuals come into effective contact with other older individuals (β_2). An effective contact is defined as one that is sufficient to lead to transmission if it occurs between a susceptible and infectious person[70]. The rate at which younger and older individuals come into effective contact is assumed to be 70% of the rate at which older individuals effectively contact each other, which is consistent with empirical data from middle-income settings[71], which are typical of those which were likely to have introduced rubella-containing vaccination. Recent studies

suggest that the rate at which children and adults contact each other estimated in these studies is likely to be similar elsewhere[72].

The contact parameters in the model for each country were calculated for each bootstrap estimate for the force of infection for younger and older individuals, before the introduction of vaccination using standard methods (see below)[73]. For a given assumption about contact between individuals, the force of infection at time *t* for individuals among younger and older individuals ($\lambda_y(t)$ and $\lambda_o(t)$ respectively), is given by the following equations:

Stable populations with rectangular age distribution:

$$\lambda_y(t) = \beta_{yy} I_y(t) + \beta_{yo} I_o(t)$$
$$\lambda_o(t) = \beta_{oy} I_y(t) + \beta_{oo} I_o(t)$$

Growing populations:

$$\lambda_y(t) = \frac{c_{yy} I_y(t) + c_{yo} I_o(t)}{N_y(t)}$$
$$\lambda_o(t) = \frac{c_{oy} I_y(t) + c_{oo} I_o(t)}{N_o(t)}$$

c_{yy}, c_{yo}, c_{oy} and c_{oo} are related to β_{yy}, β_{yo}, β_{oy} and β_{oo} through the following equations, where T_0 is the start of the model runs:

$$c_{yy} = \beta_{yy} N_y(T_0)$$
$$c_{yo} = \beta_{yo} N_y(T_0)$$
$$c_{oy} = \beta_{oy} N_o(T_0)$$
$$c_{oo} = \beta_{oo} N_o(T_0)$$

The parameters, β_1 and β_2 in the WAIFW matrix for given values for the average force of infection before the introduction of vaccination among younger and older individuals for a given country (denoted by $\bar{\lambda}_y$ and $\bar{\lambda}_o$ respectively) were calculated using the following equations:

$$\beta_1 = \frac{\bar{\lambda}_y - 0.7\beta_2 \bar{I}_o}{\bar{I}_y}$$

$$\beta_2 = \frac{0.7\bar{\lambda}_y}{0.7\bar{I}_y + \bar{I}_o}$$

where $\bar{I}_y$ and $\bar{I}_o$ are the average numbers of infectious individuals (males and females combined) for younger and older individuals, respectively. These equations are obtained after rearranging the following equation, which relates the force of infection to the number of infectious younger and older individuals:

$$\begin{pmatrix} \beta_1 & 0.7\beta_2 \\ 0.7\beta_2 & \beta_2 \end{pmatrix} \begin{pmatrix} \bar{I}_y \\ \bar{I}_o \end{pmatrix} = \begin{pmatrix} \bar{\lambda}_y \\ \bar{\lambda}_o \end{pmatrix}$$

The calculations of the contact parameters implicitly assume that the seroprevalence data were representative of the seroprevalence in the general population at any given time, and therefore that the average annual force of infection and contact parameters estimated from these data are also representative of those in the general population. $\bar{I}_y$ and $\bar{I}_o$ are calculated using the approximations $\bar{I}_y \approx \bar{\lambda}_y \bar{S}_y D$ and $\bar{I}_o \approx \bar{\lambda}_o \bar{S}_o D$, where D is the duration of infectiousness and $\bar{S}_y$ and $\bar{S}_o$ are the average numbers of susceptible children and older individuals respectively. For populations with a rectangular age distribution, $\bar{S}_y$ and $\bar{S}_o$ are given by:

$$\bar{S}_y = \frac{N(e^{-\bar{\lambda}_y 0.5} - e^{-\bar{\lambda}_y a_y})}{\bar{\lambda}_y L}$$

$$\bar{S}_o = \frac{N e^{-\bar{\lambda}_y (a_y - 0.5)}(1 - e^{-\bar{\lambda}_o (L - a_y)})}{\bar{\lambda}_o L}$$

where N is the total population size, a_y (=13 years) is the oldest age of young individuals and L is the life expectancy (75 years).

For growing populations, the equations are as follows:

$$\overline{S_y} = \sum_{a=1}^{a_y} N_a(T_0) e^{-\bar{\lambda}_y (a-0.5)}$$

$$\overline{S_o} = \sum_{a=a_y}^{75} N_a(T_0) e^{-12.5\bar{\lambda}_y} e^{-\bar{\lambda}_o (a-a_y)}$$

Here, the number of people of age *a* was calculated using the following equation, namely by multiplying the population size at the start ($N_a(T_0)$) by the proportion of the population at equilibrium that was of age *a:*

$$N_a(T_0) = N(T_0) \frac{N_a(T_E)}{\sum_{a=0}^{75} N_a(T_E)}$$

The equilibrium numbers of people in each age group were obtained by running the model until it reached 2010 and therefore takes account of age-dependent mortality rates and the survival of people.

3.4 Vaccination coverage data

The vaccination coverage data that were used in the model are described in the main text. Missing SIA or routine coverage data were further supplemented from publications[74-93]. Data on “selective vaccination” coverage came from publications where possible[94-96] (see main text for details).

D: Results from fitting catalytic models to the serological data collected before the introduction of RCV

Table H: Summary of the studies, best-fitting values for the force of infection and (where appropriate) the sensitivity of the antibody assay, and the CRS incidence per 100,000 live births for each catalytic model, for settings in which rubella vaccine had not been introduced by 2010. The values in parentheses reflect the 95% confidence intervals, obtained by bootstrapping. To facilitate comparisons, the CRS incidence is not weighted by the number of live births.

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
					<13 yr olds	≥13 yr olds					1	2
Africa												
Benin, 1993[5]	Pregnant F	211 (4)	HAI-?	A	0 (0,968)	652 (0,928)	86 (82,100)	170 (0,391)	0.3 (1)	--		
				B	156 (91,181)	0 (0,52)	-	0 (0,149)	0.4 (2)	29		
				C	329 (89,985)	329 (89,985)	86 (81,94)	6 (0,173)	0.4 (2)	29		
				D	69 (58,82)	69 (58,82)	-	217 (187,240)	6.9 (3)	23	D	D
Congo, <1991[6]	Pregnant F	100 (6)	HAI-1:20	A	0 (0,214)	378 (59,833)	89 (82,100)	306 (6,420)	3.6 (3)	36		
				B	118 (12,184)	32 (0,161)	-	88 (0,408)	7.2 (4)	30		
				C	121 (76,769)	121 (76,769)	90 (82,100)	113 (0,202)	5.7 (4)	28		
				D	75 (59,99)	75 (59,99)	-	205 (153,238)	8.3 (5)	26	B	D
Cote d'Ivoire, 1975[7]	Pregnant F	4952 (5)	HAI-1:10	A	131 (86,148)	183 (39,504)	89 (86,100)	90 (62,127)	2.2 (2)	63		
				B	116 (105,127)	48 (32,64)	--	110 (81,136)	3.7 (3)	44		
				C	135 (115,162)	135 (115,162)	90 (88,94)	94 (63,123)	2.3 (3)	43		
				D	90 (87,94)	90 (87,94)	--	171 (163,177)	31.1 (4)	65	B	D
Cote d'Ivoire, 1984-6[97]	Pregnant F	1143 (3)	HAI:1:20	A	447 (66,991)	0 (0,860)	60 (57,100)	0 (0,56)	1.3 (0)	--	D dropped – poor fit	D dropped – poor fit
				B	72 (65,77)	0 (0,6)	--	0 (0,48)	1.3 (1)	--		
				C	925 (174,999)	925 (174,999)	59 (57,62)	0 (0,54)	1.3 (1)	--		
				D	35 (32,37)	35 (32,37)	--	263 (261,264)	58 (2)	82		

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
					<13 yr olds	≥13 yr olds					1	2
Cote d'Ivoire, 1985-6[8]	Random sera samples M & F	2524 (9)	HAI-1:10	A	156 (74,191)	1000 (0,1000)	61 (60,100)	11 (0,44)	12.3 (6)	74	C	C
				B	75 (70,79)	0 (0,5)	--	0 (0,37)	14.5 (7)	72		
				C	170 (140,215)	170 (140,215)	62 (60,65)	57 (29,87)	16.5 (7)	74		
				D	38 (36,40)	38 (36,40)	--	264 (263,264)	170 (8)	224		
Ethiopia , 1981[9]	Pregnant F	137 (6)	HAI-1:16	A	137 (0,264)	99 (1,989)	100 (92,100)	95 (0,275)	2.2 (3)	33	B	D
				B	137 (29,241)	99 (0,295)	--	95 (0,253)	2.2 (4)	23		
				C	122 (100,997)	122 (100,997)	100 (91,100)	113 (0,151)	2.3 (4)	23		
				D	122 (98,162)	122 (98,162)	--	113 (64,155)	2.3 (5)	18		
Ethiopia (Addis Ababa), 1994[10]	Urban F population	2809 (50)	RH, EIA & LA	A	261 (230,295)	83 (23,164)	98 (96,100)	20 (12,28)	75.2 (47)	194	A	A
				B	233 (215,252)	26 (9,47)	--	19 (7,30)	78.4 (48)	195		
				C	269 (237,305)	269 (237,305)	96 (96,97)	13 (8,21)	79.3 (48)	196		
				D	169 (158,183)	169 (158,183)	--	57 (47,67)	206.9 (49)	321		
Gabon, 1985[11]	Pregnant F	1737 (4)	HAI-1:40	A	17 (0,82)	546 (24,1000)	78 (76,100)	173 (69,268)	5.6 (1)	--	B	C
				B	79 (66,91)	21 (14,29)	--	113 (71,159)	17.4 (2)	56		
				C	87 (70,109)	87 (70,109)	83 (79,87)	177 (134,215)	14.3 (2)	53		
				D	44 (42,47)	44 (42,47)	--	261 (257,263)	52.3 (3)	79		

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
Ghana, 1997[12]	Pregnant F	404 (3)	SRH	A	120 (58,200)	60 (10,589)	100 (93,100)	112 (14,215)	0.9 (0)	--	B	D
				B	120 (71,196)	60 (10,100)	--	112 (14,215)	0.9 (1)	--		
				C	116 (78,993)	116 (78,993)	96 (91,100)	122 (0,196)	1.6 (1)	--		
				D	85 (75,99)	85 (75,99)	--	181 (152,204)	2.3 (2)	19		
Kenya (Kilifi), 1996-9[2-3]	Pregnant F	276 (5)	EIA	A	79 (0,126)	91 (22,678)	89 (75,100)	195 (70,333)	0.3 (2)	50	B	D
				B	73 (42,107)	45 (11,87)	--	183 (50,310)	0.5 (3)	30		
				C	80 (56,170)	80 (56,170)	90 (76,100)	192 (57,244)	0.3 (3)	30		
				D	61 (51,71)	61 (51,71)	--	235 (214,252)	1.1 (4)	24		
Madagascar, 1990-1995[13]	Pregnant F	567 (6)	EIA, ELFA, HAI	A	0 (0,176)	501 (4,857)	80 (77,100)	235 (6,357)	4.3 (3)	48	B	B
				B	104 (73,135)	17 (0,42)	--	71 (0,181)	5.2 (4)	39		
				C	131 (72,935)	131 (72,935)	82 (77,92)	99 (0,210)	5.2 (4)	39		
				D	55 (50,62)	55 (50,62)	--	245 (232,254)	13.3 (5)	42		
Mozambique, 2002[14]	Pregnant F	962 (3)	EIA	A	211 (0,282)	164 (11,1000)	97 (95,100)	34 (7,106)	0 (0)	--	B	D
				B	209 (173,251)	39 (1,88)	--	31 (1,61)	0.4 (1)	--		
				C	202 (160,885)	202 (160,885)	97 (95,99)	36 (0,66)	0 (1)	--		
				D	136 (123,153)	136 (123,153)	--	92 (73,110)	18.4 (2)	38		
Niger, <1991[98]	Pregnant F	345 (3)	?	A	957 (8,994)	852 (0,997)	71 (67,96)	0 (0,75)	4.7 (0)	--	D dropped – poor fit	D dropped – poor fit
				B	98 (87,113)	0 (0,0)	--	0 (0,0)	4.7 (1)	--		
				C	991 (293,999)	991 (293,999)	71 (66,76)	0 (0,9)	4.7 (1)	--		
				D	50 (43,57)	50 (43,57)	--	254 (242,261)	32.8 (2)	53		

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
Nigeria, <1978[15]	Sera from F in Obs. & Gynae.	500 (5)	HAI-?	A	0 (0,100)	455 (17,828)	75 (71,100)	259 (55,349)	2.6 (2)	55	B	C
				B	87 (62,107)	18 (0,48)	--	90 (0,208)	5.1 (3)	38		
				C	124 (72,401)	124 (72,401)	77 (70,90)	109 (2,210)	4.3 (3)	37		
				D	55 (49,62)	55 (49,62)	--	246 (233,255)	12.7 (4)	39		
Nigeria, <2002[16]	Pregnant F	207 (5)	EIA	A	4 (0,23)	78 (41,168)	88 (68,100)	496 (334,526)	1.725 (2)	52	C	D
				B	7 (0,26)	57 (37,74)	--	449 (305,518)	1.872 (3)	32		
				C	32 (26,38)	32 (26,38)	100 (100,100)	260 (250,264)	7.986 (3)	38		
				D	32 (26,38)	32 (26,38)	--	260 (250,264)	7.986 (4)	31		
Nigeria, 2007-8 [17]	Pregnant F	404 (4)	EIA	A	312 (0,994)	0 (0,979)	100 (96,100)	0 (0,241)	3.8 (1)	--	D	D
				B	296 (249,351)	0 (0,35)	--	0 (0,13)	3.8 (2)	31		
				C	806 (206,949)	806 (206,949)	98 (96,99)	0 (0,34)	3.8 (2)	31		
				D	131 (113,162)	131 (113,162)	--	98 (63,127)	15.3 (3)	30		
Senegal, 1996-2001[18]	F (child-bearing age)	3471 (6)	EIA	A	173 (0,859)	9 (0,1000)	100 (90,100)	18 (0,124)	2 (3)	53	B	B
				B	173 (151,189)	9 (0,26)	--	18 (0,52)	2 (4)	43		
				C	259 (153,979)	259 (153,979)	90 (89,92)	15 (0,72)	3.1 (4)	44		
				D	81 (78,85)	81 (78,85)	--	190 (181,197)	75 (5)	111		
South Africa, 2003[19]	Pregnant F	1200 (3)	EIA	A	213 (0,275)	149 (16,989)	98 (97,100)	34 (9,153)	0 (0)	--	B	D
				B	222 (177,271)	48 (4,106)	--	29 (3,57)	0.3 (1)	--		
				C	197 (159,337)	197 (159,337)	98 (96,99)	38 (5,67)	0 (1)	--		

				D	146 (132,165)	146 (132,165)	--	80 (61,98)	13.9 (2)	32		
Country, year of study	**Study population**	**Sample size (no. of age groups)**	**Lab test (cut-off)**	**Cata-lytic model**	**Force of infection (/1000/year)**		**Sensitivity (%)**	**CRS/ 100,000 live births**	**Loglike-lihood deviance (deg of freedom)**	**AICc**	**Selected model based on criterion:**	
Zambia, 1979-80[20]	F post-partum	100 (6)	RH & HAI-1:10	A	97 (26,178)	84 (20,266)	100 (96,100)	157 (35,317)	3.2 (5)	32	A	D
				B	97 (32,178)	84 (19,192)	--	157 (33,317)	3.2 (5)	22		
				C	91 (72,996)	91 (72,996)	100 (87,100)	169 (0,210)	3.2 (5)	22		
				D	91 (72,121)	91 (72,121)	--	169 (113,211)	3.2 (5)	17		
Eastern Mediterranean												
Pakistan, <1997 [37]	General pop. (M/F?)	300 (6)	EIA	A	178 (103,338)	136 (25,1000)	84 (74,100)	54 (2,141)	6.3 (3)	49	B	C
				B	118 (95,144)	27 (0,74)	--	81 (0,151)	8.1 (4)	41		
				C	182 (110,344)	182 (110,344)	83 (74,94)	48 (4,132)	6.3 (4)	39		
				D	93 (79,110)	93 (79,110)	--	165 (131,194)	16.1 (5)	43		
Pakistan, 1999-2004[38]	Pregnant F	1163 (5)	EIA	A	144 (0,952)	8 (0,1000)	100 (84,100)	24 (0,128)	16.1 (2)	70	B	B
				B	144 (122,161)	8 (0,28)	--	24 (0,77)	16.1 (3)	50		
				C	559 (137,995)	559 (137,995)	85 (83,89)	0 (0,91)	16.6 (3)	51		
				D	74 (68,79)	74 (68,79)	--	207 (194,218)	45.8 (4)	73		
Yemen, 1985[42]	Residual sera?	476 (6)	HAI-?	A	255 (179,364)	169 (104,1000)	85 (80,91)	20 (2,52)	13.3 (3)	57	C	C
				B	163 (139,185)	0 (0,40)	--	0 (0,68)	20.4 (4)	54		
				C	258 (183,365)	258 (183,365)	85 (80,90)	16 (3,47)	13.3 (4)	47		
				D	116 (100,134)	116 (100,134)	--	122 (95,151)	45.4 (5)	74		

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
Yemen, 2002-03[43]	Unvaccinated pop. (M/F?)	1253 (5)	EIA	A	192 (174,216)	22 (9,1000)	100 (95,100)	28 (6,45)	11.1 (2)	66	B	B
				B	192 (174,212)	22 (9,42)	--	28 (12,47)	11.1 (3)	46		
				C	206 (182,235)	206 (182,235)	96 (95,98)	33 (22,48)	12.8 (3)	47		
				D	149 (135,166)	149 (135,166)	--	76 (60,93)	71.5 (4)	99		
South East Asia												
Bangladesh, 2004-05[53]	F aged 1-45 yrs	582 (9)	HAI? – 1:10	A	110 (84,143)	59 (22,1000)	93 (82,100)	126 (18,168)	1.7 (6)	50	B	B
				B	99 (82,120)	35 (16,54)	--	118 (59,169)	1.8 (7)	45		
				C	117 (88,157)	117 (88,157)	88 (83,94)	121 (69,174)	2 (7)	45		
				D	70 (62,79)	70 (62,79)	--	215 (194,232)	16.6 (8)	56		
India (urban Delhi), 1968[54]	15-34+ year old F	217 (5)	HAI	A	160 (103,325)	64 (0,1000)	91 (80,100)	69 (0,137)	0.2 (2)	49	B	B
				B	129 (99,158)	27 (0,85)	--	70 (0,140)	0.4 (3)	29		
				C	178 (108,349)	178 (108,349)	87 (79,98)	50 (4,136)	0.4 (3)	29		
				D	97 (80,118)	97 (80,118)	--	157 (118,193)	7.5 (4)	30		
India (rural Delhi), 1968[54]	15-34+ year old F	204 (5)	HAI	A	85 (66,177)	19 (0,1000)	100 (68,100)	96 (0,204)	0.7 (2)	51	B	D
				B	85 (63,109)	19 (0,60)	--	96 (0,218)	0.7 (3)	31		
				C	127 (68,217)	127 (68,217)	77 (67,97)	105 (29,218)	1.2 (3)	31		
				D	64 (53,77)	64 (53,77)	--	228 (199,249)	6.3 (4)	30		

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
India (Chandrigarh), 1972-3[54]	15-34+ year old F	365 (6)	HAI	A	134 (115,518)	0 (0,1000)	100 (78,100)	0 (0,47)	3.3 (3)	44	C	C
				B	133 (114,151)	0 (0,17)	--	0 (0,56)	3.3 (4)	34		
				C	244 (159,543)	244 (159,543)	81 (77,86)	19 (0,66)	4.5 (4)	35		
				D	74 (65,85)	74 (65,85)	--	205 (182,227)	29.6 (5)	55		
India (Lucknow), 1972-3[54]	15-34+ year old F	412 (6)	HAI	A	133 (91,206)	201 (69,635)	89 (85,96)	85 (25,145)	2.6 (3)	45	B	C
				B	123 (97,154)	32 (5,63)	--	83 (13,148)	5.6 (4)	38		
				C	140 (105,211)	140 (105,211)	90 (85,95)	87 (31,141)	2.9 (4)	35		
				D	82 (71,94)	82 (71,94)	--	189 (162,212)	19 (5)	46		
India (Calcutta), 1976[55]	Patients at skin clinics, mothers & babies	344 (7)	?	A	226 (111,1000)	460 (79,1000)	65 (56,76)	15 (0,111)	17 (4)	60	B	B
				B	82 (66,98)	8 (0,26)	--	49 (0,143)	28.6 (5)	65		
				C	231 (117,1000)	231 (117,1000)	65 (56,75)	23 (0,120)	17 (5)	53		
				D	50 (43,59)	50 (43,59)	--	254 (238,262)	51.7 (6)	84		
India (Delhi), <1987[56]	Pregnant F	160 (5)	?	A	54 (18,1000)	9 (0,1000)	100 (47,100)	77 (0,320)	5.9 (2)	54	B	D
				B	54 (27,73)	9 (0,41)	--	77 (0,306)	5.9 (3)	34		
				C	255 (29,1000)	255 (29,1000)	54 (46,100)	17 (0,264)	6.2 (3)	34		
				D	33 (26,41)	33 (26,41)	--	262 (250,264)	8.1 (4)	30		

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
India (Delhi), <1990[57]	Random selection of F	99 (3)	RH & HAI	A	34 (0,137)	71 (0,740)	100 (58,100)	338 (0,508)	0.1 (0)	--	D	D
				B	34 (0,79)	71 (0,145)	--	338 (0,512)	0.1 (1)	--		
				C	47 (36,992)	47 (36,992)	100 (57,100)	258 (0,264)	0.4 (1)	--		
				D	47 (36,61)	47 (36,61)	--	258 (235,264)	0.4 (2)	18		
India (rural Vellore), 1999-2000[1]	rural F	1693 (39)	EIA (serum & saliva): <4IU/ml for serum	A	116 (102,127)	224 (60,553)	93 (91,100)	100 (49,138)	87.8 (36)	220	B	C
				B	112 (102,123)	72 (55,92)	--	127 (107,147)	90.9 (37)	221		
				C	117 (105,130)	117 (105,130)	96 (94,99)	120 (100,141)	89.6 (37)	219		
				D	99 (93,106)	99 (93,106)	--	153 (140,165)	99.2 (38)	227		
India (urban Vellore), 1999-2000 [1]	urban F	1409 (39)	EIA (serum & saliva): <4IU/ml for serum	A	175 (154,197)	206 (60,1000)	97 (95,100)	50 (8,69)	51.3 (36)	155	B	C
				B	170 (153,190)	67 (39,104)	--	61 (42,77)	54.8 (37)	156		
				C	176 (156,200)	176 (156,200)	97 (96,99)	52 (37,70)	51.4 (37)	153		
				D	140 (129,154)	140 (129,154)	--	87 (71,102)	77.3 (38)	177		

Country, year of study	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model based on criterion:	
Nepal, 2008[58]	outpatient F aged 15 -39 yrs	2224 (5)	EIA: <10IU	A	0 (0,308)	988 (0,1000)	91 (90,100)	82 (0,139)	4.8 (2)	62	B	B
				B	180 (157,199)	9 (0,31)	--	17 (0,52)	7.6 (3)	45		
				C	225 (168,939)	225 (168,939)	91 (90,93)	25 (0,58)	6.3 (3)	44		
				D	94 (89,100)	94 (89,100)	--	163 (151,174)	82.4 (4)	113		
Western Pacific												
Central Vietnam, 2009-2010[65]	pregnant F	1988 (23)	EIA: <4 IU/ml	A	51 (0,67)	40 (28,215)	100 (75,100)	227 (158,479)	29.7 (20)	141	A	D
				B	52 (36,69)	40 (25,53)	--	227 (146,308)	29.7 (21)	138		
				C	52 (43,77)	52 (43,77)	93 (81,100)	250 (199,261)	29.8 (21)	138		
				D	45 (43,48)	45 (43,48)	--	260 (257,262)	30.4 (22)	136		

Notes:
Types of catalytic model: A- full model (force of infection among younger and older individuals and test sensitivity are estimated; B-similar to version used in previous analyses[99] (force of infection among younger and older individuals estimated, sensitivity=100%); C-force of infection is assumed to be age-independent, and is estimated, as is the test sensitivity; D- force of infection is assumed to be age-independent, and is estimated, test sensitivity=100%
Population:
F-females, M-males;
Type of assay used
LA: latex agglutination; EIA: enzyme-based immunoassay; MEIA: micro enzyme immunoassay; HAI: hemagglutination inhibition; RH: Radial haemolysis

Table I: Summary of the studies, best-fitting values for the force of infection predating the introduction of vaccination and (where appropriate) the sensitivity of the antibody assay, and the CRS incidence per 100,000 live births for each catalytic model, for settings in which rubella vaccine had not been introduced by 2010. The values in parentheses reflect the 95% confidence intervals, obtained by bootstrapping. To facilitate comparisons, the infection and CRS incidence is not weighted by the number of live births.

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
America												
Argentina (urban), 1967-68[21]	Sera from urban & rural M&F	491 (5)	HAI-1:10	A	213 (123,415)	40 (0,395)	86 (80,100)	31 (0,90)	2 (2)	55	A	C
				B	137 (113,154)	5 (0,35)	--	16 (0,97)	3.2 (3)	36		
				C	246 (154,442)	246 (154,442)	83 (79,88)	19 (1,71)	2.7 (3)	35		
				D	90 (79,102)	90 (79,102)	--	172 (147,194)	27.5 (4)	53		
Argentina (rural), 1967-68[21]	Sera from urban & rural M&F	129 (5)	HAI-1:10	A	156 (92,1000)	54 (0,131)	94 (81,100)	69 (0,163)	5.1 (2)	50	B	D
				B	130 (92,178)	36 (0,103)	--	81 (0,163)	5.2 (3)	30		
				C	190 (91,1000)	190 (91,1000)	88 (79,100)	42 (0,169)	5.8 (3)	31		
				D	97 (78,127)	97 (78,127)	--	156 (104,196)	8 (4)	26		
Argentina (Mar de Plata), 1981[22]	Gen popn F going to health checks	769 (5)	HAI-1:8	A	695 (44,977)	0 (0,1000)	88 (87,100)	0 (0,67)	1 (2)	52	D	D
				B	172 (147,186)	0 (0,28)	--	0 (0,56)	1 (3)	32		
				C	970 (199,999)	970 (199,999)	88 (86,91)	0 (0,37)	1 (3)	32		
				D	99 (91,110)	99 (91,110)	--	152 (133,170)	28.3 (4)	52		
Brazil, 1967-68[21]	Sera from urban & rural M&F	295 (6)	HAI-1:10	A	163 (132,229)	12 (0,1000)	100 (90,100)	26 (0,81)	4.6 (3)	44	B	B
				B	163 (133,193)	12 (0,51)	--	26 (0,83)	4.6 (4)	34		
				C	208 (145,301)	208 (145,301)	90 (86,95)	33 (8,81)	6.9 (4)	36		
				D	103 (88,124)	103 (88,124)	--	144 (109,175)	26.1 (5)	50		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Brazil, 1987[23]	Residual sera (children), & cord blood (adults)	1729 (11)	EIA	A	131 (117,154)	88 (50,278)	97 (91,100)	102 (62,120)	16.8 (8)	80	A	B
				B	126 (116,136)	68 (43,100)	--	107 (86,122)	16.9 (9)	77		
				C	137 (121,157)	137 (121,157)	95 (91,99)	91 (69,114)	17.2 (9)	77		
				D	118 (110,127)	118 (110,127)	--	118 (105,132)	25.7 (10)	82		
Brazil (Parana), 1996-8[24]	Pregnant F	1348 (3)	EIA	A	203 (139,996)	1000 (0,1000)	90 (88,99)	6 (0,50)	0.2 (0)	-	B	D
				B	172 (149,189)	6 (0,26)	--	13 (0,51)	1.3 (1)	-		
				C	238 (177,999)	238 (177,999)	90 (88,92)	21 (0,52)	0.4 (1)	-		
				D	89 (83,97)	89 (83,97)	--	172 (157,185)	70.5 (2)	93		
Canada, <1967 [25]	Residual sera	198 (5)	HAI-?	A	111 (72,154)	179 (47,1000)	93 (85,100)	116 (13,201)	0.3 (2)	48	B	D
				B	100 (71,135)	76 (30,145)	--	148 (77,208)	0.6 (3)	28		
				C	108 (81,162)	108 (81,162)	96 (87,100)	136 (64,191)	0.5 (3)	28		
				D	93 (78,114)	93 (78,114)	--	165 (125,196)	1.1 (4)	22		
Chile (Santiago), 1967-68[21]	Sera from urban M&F	281 (5)	HAI-1:10	A	1000 (389,1000)	104 (24,163)	97 (95,99)	0 (0,4)	12.8 (2)	51	B	B
				B	303 (240,408)	27 (0,86)	--	8 (0,25)	19.7 (3)	38		
				C	1000 (448,1000)	1000 (448,1000)	97 (95,99)	0 (0,1)	12.8 (3)	31		
				D	226 (183,312)	226 (183,312)	--	25 (7,47)	26.8 (4)	38		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Chile (rural), 1967-68[21]	Sera from rural M&F	163 (5)	HAI-1:10	A	370 (271,584)	1000 (1000,1000)	100 (100,100)	1 (0,3)	1.1 (2)	34	C	D
				B	370 (271,584)	1000 (1000,1000)	--	1 (0,3)	1.1 (3)	14		
				C	381 (293,586)	381 (293,586)	100 (100,100)	3 (0,9)	1.3 (3)	14		
				D	381 (293,586)	381 (293,586)	--	3 (0,9)	1.3 (4)	8		
Haiti, 2002[29]	Pregnant F (urban)	425 (6)	EIA	A	42 (0,883)	1000 (0,1000)	96 (95,100)	48 (0,153)	1.4 (3)	34	B	C
				B	249 (173,292)	8 (0,90)	--	6 (0,58)	1.7 (4)	25		
				C	266 (157,999)	266 (157,999)	96 (94,99)	14 (0,68)	1.5 (4)	24		
				D	128 (109,157)	128 (109,157)	--	104 (69,133)	13.1 (5)	31		
Jamaica (Kingston), 1967-68[21]	Sera from urban M&F	200 (5)	HAI-1:10	A	1000 (267,1000)	7 (0,66)	63 (57,70)	0 (0,3)	6.7 (2)	57	D	D
				B	88 (74,105)	0 (0,0)	--	0 (0,0)	19.1 (3)	49		
				C	1000 (335,1000)	1000 (335,1000)	63 (57,69)	0 (0,5)	6.7 (3)	37		
				D	58 (49,70)	58 (49,70)	--	240 (216,255)	47.1 (4)	71		
Jamaica (rural), 1967-68[21]	Sera from rural M&F	200 (5)	HAI-1:10	A	169 (49,1000)	219 (45,958)	49 (38,75)	52 (0,255)	6.1 (2)	57	B	D
				B	46 (32,59)	11 (0,36)	--	102 (0,266)	8.7 (3)	39		
				C	170 (42,1000)	170 (42,1000)	49 (38,86)	57 (0,260)	6.2 (3)	37		
				D	35 (28,42)	35 (28,42)	--	263 (254,264)	12.8 (4)	37		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Mexico, 1987-88[26]	Sera from blood collection	24331 (7)	HAI-1:8	A	133 (125,139)	101 (72,134)	89 (87,91)	100 (90,109)	1 (4)	-40	A	C
				B	107 (104,110)	32 (29,35)	--	102 (94,110)	23 (5)	-25		
				C	134 (128,141)	134 (128,141)	87 (87,88)	95 (86,104)	5 (5)	-43		
				D	76 (75,78)	76 (75,78)	--	201 (198,204)	799.8 (6)	747		
Mexico, 1989[27]	F of reproductive age	428 (6)	HAI:1:8	A	31 (17,48)	51 (35,85)	100 (86,100)	326 (233,416)	2.1 (3)	46	C	D
				B	31 (17,47)	51 (34,69)	--	326 (231,412)	2.1 (4)	36		
				C	40 (36,48)	40 (36,48)	100 (92,100)	263 (257,264)	3.8 (4)	38		
				D	40 (36,46)	40 (36,46)	--	263 (259,264)	3.8 (5)	33		
Panama (Panama City), 1967-68[21]	Sera from urban M&F	240 (6)	HAI-1:10	A	67 (49,144)	18 (2,1000)	100 (65,100)	56 (46,84)	2.7 (3)	45	B	B
				B	67 (49,86)	18 (0,39)	--	56 (46,66)	2.7 (4)	35		
				C	104 (48,206)	104 (48,206)	72 (62,98)	73 (45,92)	4.3 (4)	36		
				D	45 (38,54)	45 (38,54)	--	43 (38,49)	10.2 (5)	37		
Panama (rural), 1967-68[21]	Sera from rural M&F	268 (6)	HAI-1:10	A	21 (13,36)	25 (14,153)	100 (54,100)	23 (15,36)	0 (3)	48	C	D
				B	21 (13,30)	25 (14,37)	--	23 (15,32)	5.9 (4)	38		
				C	22 (18,48)	22 (18,48)	100 (61,100)	24 (20,45)	6.1 (4)	38		
				D	22 (18,27)	22 (18,27)	--	24 (20,29)	6.1 (5)	33		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Peru (Lima), 1967-68[21]	Sera from urban M&F	243 (5)	HAI-1:10	A	302 (149,1000)	0 (0,4)	83 (76,100)	0 (0,0)	15.4 (2)	64	D	C
				B	143 (122,169)	0 (0,0)	--	0 (0,0)	18.6 (3)	47		
				C	385 (265,1000)	385 (265,1000)	81 (75,86)	2 (0,14)	16.2 (3)	45		
				D	93 (79,113)	93 (79,113)	--	165 (128,195)	60.9 (4)	83		
Peru (rural), 1967-68[21]	Sera from M&F	203 (5)	EIA	A	31 (19,48)	62 (38,138)	100 (75,100)	342 (242,413)	2.2 (2)	51	C	D
				B	31 (19,44)	62 (36,89)	--	342 (245,413)	2.2 (3)	31		
				C	41 (33,50)	41 (33,50)	100 (99,100)	263 (253,264)	4.7 (3)	34		
				D	41 (33,49)	41 (33,49)	--	263 (255,264)	4.7 (4)	27		
Peru, 2003[28]	Postpartum F	1236 (7)	HAI-1:10	A	99 (0,155)	325 (19,877)	89 (87,100)	100 (44,208)	6.4 (4)	46	B	C
				B	132 (110,156)	33 (11,56)	--	76 (27,121)	6.8 (5)	39		
				C	145 (113,217)	145 (113,217)	91 (88,94)	81 (28,127)	6.6 (5)	39		
				D	86 (80,92)	86 (80,92)	--	180 (166,193)	25.6 (6)	54		
Trinidad, 1966-7[30]	Sera from M & F	71 (2)	?	A	0 (0,5)	36 (24,78)	100 (68,100)	416 (332,501)	1 (-1)	--	C	C
				B	0 (0,11)	36 (21,53)	--	416 (289,482)	1 (0)	--		
				C	19 (13,27)	19 (13,27)	100 (100,100)	221 (179,252)	4.8 (0)	--		
				D	19 (13,27)	19 (13,27)	--	221 (179,252)	4.8 (1)	--		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Trinidad (Port au Spain), 1967-68[21]	Sera from urban M&F	200 (5)	HAI-1:10	A	57 (17,305)	33 (0,1000)	54 (29,100)	193 (0,315)	0.3 (2)	50	B	D
				B	27 (15,37)	10 (0,29)	--	119 (0,290)	0.4 (3)	30		
				C	78 (18,341)	78 (18,341)	43 (28,100)	198 (5,264)	0.4 (3)	30		
				D	21 (16,27)	21 (16,27)	--	232 (201,251)	2.2 (4)	25		
Trinidad (rural), 1967-8[21]	Sera from rural M&F	200 (5)	HAI-1:10	A	22 (12,160)	9 (0,1000)	100 (28,100)	121 (0,285)	3.6 (2)	52	B	D
				B	22 (12,30)	9 (0,26)	--	121 (0,284)	3.6 (3)	32		
				C	52 (14,240)	52 (14,240)	45 (25,100)	250 (20,264)	4.2 (3)	33		
				D	17 (12,23)	17 (12,23)	--	212 (174,238)	4.8 (4)	27		
Uruguay (urban) 1967-68[21]	Sera from urban M&F	270 (6)	HAI-1:10	A	297 (156,999)	54 (0,105)	87 (81,100)	12 (0,58)	10.1 (3)	49	D	C
				B	162 (133,187)	0 (0,34)	--	0 (0,69)	13 (4)	42		
				C	329 (190,999)	329 (190,999)	85 (80,91)	6 (0,42)	10.6 (4)	40		
				D	100 (84,120)	100 (84,120)	--	151 (115,184)	42.8 (5)	67		
Uruguay (rural) 1967-68[21]	Sera from rural M&F	155 (4)	HAI-1:10	A	0 (0,965)	781 (0,1000)	88 (83,100)	129 (0,271)	0.4 (1)	-	B	D
				B	155 (97,192)	4 (0,58)	--	10 (0,144)	1.1 (2)	31		
				C	200 (102,997)	200 (102,997)	88 (83,96)	37 (0,147)	0.8 (2)	30		
				D	77 (64,98)	77 (64,98)	--	200 (155,229)	9.6 (3)	27		
USA (Atlanta), <1967[25]	Residual sera	172 (5)	HAI-?	A	313 (147,1000)	69 (0,1000)	86 (79,100)	10 (0,60)	0.8 (2)	48	D	C
				B	161 (127,195)	0 (0,36)	--	0 (0,70)	2.1 (3)	29		
				C	327 (175,1000)	327 (175,1000)	85 (79,92)	6 (0,53)	0.8 (3)	28		
				D	98 (80,124)	98 (80,124)	--	154 (109,193)	19.7 (4)	40		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
USA (Houston), <1967[25]	Residual sera	173 (5)	HAI-?	A	217 (109,1000)	1000 (0,1000)	82 (75,100)	5 (0,115)	1.5 (2)	49	B	C
				B	134 (97,163)	4 (0,62)	--	14 (0,140)	2.5 (3)	30		
				C	220 (117,1000)	220 (117,1000)	82 (75,93)	28 (0,120)	1.7 (3)	29		
				D	81 (67,101)	81 (67,101)	--	190 (149,222)	11.5 (4)	32		
Eastern Mediterranean												
Bahrain, 1981[31]	School children and pregnant F	6097 (8)	HAI-1:8	A	107 (100,114)	857 (522,1000)	88 (87,89)	29 (20,60)	59.4 (5)	124	B	C
				B	102 (97,107)	57 (47,68)	--	138 (123,150)	160.6 (6)	219		
				C	114 (107,121)	114 (107,121)	93 (92,95)	126 (114,138)	148.4 (6)	207		
				D	91 (88,95)	91 (88,95)	--	168 (161,175)	202.1 (7)	257		
Iran, 1993-95[32]	Pregnant F	2006 (11)	EIA	A	173 (148,201)	248 (99,964)	96 (94,99)	46 (10,74)	69.8 (9)	124	B	C
				B	163 (145,183)	69 (45,95)	--	67 (47,85)	76.4 (9)	127		
				C	174 (151,203)	174 (151,203)	96 (95,98)	53 (35,75)	70.3 (9)	120		
				D	130 (121,142)	130 (121,142)	--	100 (85,114)	101 (9)	148		
Jordan, 1982-3[33]	Cord blood, well child and ANC attendees	1100 (6)	EIA	A	1000 (1000,1000)	27 (6,47)	84 (82,86)	0 (0,0)	135.4 (3)	181	D	D
				B	166 (153,182)	0 (0,0)	--	0 (0,0)	301.7 (4)	337		
				C	1000 (1000,1000)	1000 (1000,1000)	84 (82,86)	0 (0,0)	135.4 (4)	171		
				D	124 (113,136)	124 (113,136)	--	110 (92,126)	374.9 (5)	405		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Kuwait, <1978[34]	F (child-bearing age)	1002 (5)	HAI-1:4	A	214 (0,658)	222 (0,941)	95 (94,100)	30 (0,189)	1.7 (2)	52	B	C
				B	217 (168,250)	15 (0,68)	--	16 (0,59)	2.1 (3)	32		
				C	216 (150,987)	216 (150,987)	95 (94,98)	29 (0,75)	1.7 (3)	32		
				D	121 (110,134)	121 (110,134)	--	114 (94,132)	21.3 (4)	45		
Lebanon, 1980-81[35]	Pregnant F	65 (3)	SRH & HAI-	A	559 (0,931)	0 (0,769)	92 (86,100)	0 (0,146)	1.2 (0)	-	D	D
				B	205 (111,334)	0 (0,174)	--	0 (0,130)	1.2 (1)	-		
				C	989 (114,999)	989 (114,999)	92 (86,100)	0 (0,125)	1.2 (1)	-		
				D	118 (86,198)	118 (86,198)	--	118 (38,178)	3.4 (2)	16		
Morocco, 1969-1970[36]	Schoolgirls & pregnant F	544 (6)	HAI-1:10	A	125 (101,189)	32 (11,738)	100 (86,100)	81 (15,133)	8.6 (3)	50	A	B
				B	125 (103,152)	32 (8,57)	--	81 (24,133)	8.6 (4)	40		
				C	167 (98,999)	167 (98,999)	88 (83,96)	60 (0,155)	11.7 (4)	43		
				D	86 (77,96)	86 (77,96)	--	179 (158,199)	20.6 (5)	47		
Saudi Arabia, 1989[39]	Children in peds clinic, F at Obs. & Gynae	672 (3)	EIA	A	188 (152,397)	21 (0,1000)	100 (91,100)	29 (0,56)	0 (0)	-	B	D
				B	188 (145,219)	21 (0,79)	--	29 (0,84)	0 (1)	-		
				C	239 (161,431)	239 (161,431)	93 (91,96)	21 (1,64)	0.3 (1)	-		
				D	121 (108,136)	121 (108,136)	--	113 (92,136)	11.5 (2)	30		
Saudi Arabia, 1992-93[40]	Antenatal F	10824 (6)	?	A	180 (154,215)	103 (67,147)	93 (92,95)	55 (35,76)	23.6 (3)	81	A	D
				B	160 (149,171)	27 (17,37)	--	48 (31,64)	31.1 (4)	79		
				C	161 (144,192)	161 (144,192)	93 (92,94)	65 (41,83)	26.7 (4)	74		
				D	91 (89,94)	91 (89,94)	--	168 (163,173)	220.1 (5)	263		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Tunisia, <1970[41]	Schoolgirls & pregnant F	429 (5)	HAI-1:10	A	473 (340,1000)	208 (8,941)	94 (90,97)	1 (0,6)	3.4 (2)	50	D	C
				B	283 (248,329)	0 (0,33)	--	0 (0,12)	14.8 (3)	42		
				C	475 (342,1000)	475 (342,1000)	94 (90,97)	1 (0,5)	3.4 (3)	30		
				D	240 (203,289)	240 (203,289)	--	20 (10,35)	43 (4)	63		
Europe												
Czech Republic, <1967[25]	Residual sera	157 (5)	HAI-?	A	135 (105,463)	0 (0,1000)	100 (77,100)	0 (0,109)	1.5 (2)	48	C	C
				B	135 (101,161)	0 (0,48)	--	0 (0,116)	1.5 (3)	28		
				C	219 (122,498)	219 (122,498)	82 (75,91)	28 (0,112)	2.3 (3)	29		
				D	82 (67,101)	82 (67,101)	--	189 (149,222)	12.9 (4)	33		
Denmark, <1967[25]	Residual sera	118 (3)	HAI-?	A	235 (203,280)	15 (0,401)	96 (92,100)	13 (0,36)	12.8 (14)	93	A	C
				B	207 (192,223)	0 (0,84)	--	0 (0,41)	15 (15)	92		
				C	248 (214,289)	248 (214,289)	94 (91,98)	18 (10,30)	13.8 (15)	91		
				D	197 (183,213)	197 (183,213)	--	38 (30,47)	25.8 (16)	100		
Denmark, 1983[44]	Residual sera	1442 (17)	EIA	A	103 (0,948)	49 (0,798)	100 (83,100)	130 (0,419)	0 (0)	-	B	D
				B	103 (22,171)	49 (0,148)	--	130 (0,373)	0 (1)	-		
				C	104 (66,958)	104 (66,958)	92 (81,100)	142 (0,224)	0 (1)	-		
				D	77 (61,99)	77 (61,99)	--	200 (153,234)	0.4 (2)	17		
East Germany, 1990[45]	Random sample	1862 (23)	HAI-? (EIA on neg.)	A	205 (188,240)	82 (64,118)	100 (96,100)	41 (26,50)	29.6 (20)	119	A	B
				B	201 (187,217)	77 (50,114)	--	42 (33,50)	29.6 (21)	117		
				C	223 (193,256)	223 (193,256)	97 (94,99)	26 (16,41)	34.7 (21)	122		
				D	187 (175,202)	187 (175,202)	--	44 (36,53)	43.9 (22)	128		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
England, <1967[25]	Residual sera	294 (5)	HAI-?	A	111 (89,190)	8 (0,1000)	100 (77,100)	36 (0,134)	2.2 (2)	53	B	B
				B	111 (88,130)	8 (0,40)	--	36 (0,138)	2.2 (3)	33		
				C	162 (108,241)	162 (108,241)	80 (73,88)	64 (20,135)	3.7 (3)	35		
				D	72 (62,85)	72 (62,85)	--	211 (182,233)	18.8 (4)	43		
England, 1986-87[46]	Residual sera	4230 (44)	RH	A	126 (120,143)	62 (50,299)	100 (92,100)	105 (63,114)	57.7 (41)	231	A	B
				B	126 (119,132)	62 (50,76)	--	105 (93,117)	57.7 (42)	229		
				C	134 (125,144)	134 (125,144)	95 (93,97)	94 (83,107)	59.5 (42)	230		
				D	110 (105,115)	110 (105,115)	--	132 (123,141)	104.9 (43)	273		
Finland, 1979[47]	Sera sent for rubella test	751 (12)	RH	A	82 (72,93)	187 (141,250)	89 (88,91)	164 (138,186)	15.6 (9)	92	B	D
				B	88 (80,96)	59 (51,68)	--	166 (144,188)	52.9 (10)	126		
				C	95 (88,104)	95 (88,104)	93 (92,95)	160 (142,176)	35.7 (10)	109		
				D	74 (72,76)	74 (72,76)	--	206 (202,211)	68.2 (11)	138		
France, <1967[25]	Residual sera	201 (5)	HAI-?	A	146 (90,233)	766 (0,1000)	81 (75,100)	21 (0,128)	2.1 (2)	51	B	C
				B	110 (80,140)	17 (0,58)	--	66 (0,178)	3.8 (3)	33		
				C	149 (95,247)	149 (95,247)	83 (75,92)	76 (19,160)	2.9 (3)	32		
				D	74 (61,91)	74 (61,91)	--	205 (169,233)	12.7 (4)	35		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Kyrgyzstan, 2001[48]	F attending women's clinics	964 (5)	EIA	A	55 (0,884)	1000 (0,1000)	93 (92,100)	41 (0,140)	5.4 (2)	57	D	C
				B	210 (178,229)	0 (0,28)	--	0 (0,38)	5.7 (3)	38		
				C	362 (187,999)	362 (187,999)	93 (91,95)	3 (0,44)	5.7 (3)	38		
				D	102 (93,113)	102 (93,113)	--	147 (127,164)	46.1 (4)	71		
Romania, <1989[49]	Healthy F	5030 (5)	HAI-1:20	A	166 (144,995)	0 (0,939)	88 (76,93)	0 (0,0)	6.3 (2)	71	D	D
				B	116 (112,121)	0 (0,0)	--	0 (0,0)	6.3 (3)	51		
				C	964 (860,999)	964 (860,999)	77 (76,78)	0 (0,0)	6.3 (3)	51		
				D	54 (52,56)	54 (52,56)	--	248 (245,251)	319.4 (4)	358		
Turkey, 1998[50]	F of reproductive age	467 (6)	EIA	A	356 (19,999)	0 (0,1000)	99 (97,100)	0 (0,63)	4 (3)	34	D	D
				B	325 (261,385)	0 (0,48)	--	0 (0,15)	4 (4)	24		
				C	995 (246,999)	995 (246,999)	98 (97,99)	0 (0,19)	4 (4)	24		
				D	153 (129,199)	153 (129,199)	--	72 (37,102)	23.2 (5)	38		
Turkey, 2003-04[51]	Pregnant F	803 (6)	EIA	A	695 (31,984)	0 (0,1000)	94 (93,100)	0 (0,55)	5.6 (3)	44	D	D
				B	231 (209,255)	0 (0,1)	--	0 (0,2)	5.6 (4)	34		
				C	962 (287,999)	962 (287,999)	94 (93,96)	0 (0,10)	5.6 (4)	34		
				D	112 (101,126)	112 (101,126)	--	128 (107,149)	42.5 (5)	66		
Turkey, 2005[52]	Women attending health care centres	607 (4)	EIA	A	143 (0,985)	0 (0,1000)	66 (52,97)	0 (0,256)	1 (1)	--	D	D
				B	64 (54,71)	0 (0,6)	--	0 (0,56)	1 (2)	39		
				C	674 (116,993)	674 (116,993)	55 (51,60)	0 (0,121)	1 (2)	39		
				D	26 (24,29)	26 (24,29)	--	251 (242,257)	41.4 (3)	67		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
South East Asia												
Thailand, 1978[59]	F of childbearing age	300 (6)	HAI-1:8	A	84 (0,108)	63 (13,599)	87 (75,100)	176 (56,387)	2.9 (3)	45	A	D
				B	74 (46,105)	30 (6,56)	--	150 (33,267)	2.9 (4)	35		
				C	83 (49,184)	83 (49,184)	85 (75,100)	186 (46,255)	2.9 (4)	35		
				D	50 (44,59)	50 (44,59)	--	254 (239,261)	5.9 (5)	33		
Western Pacific												
Australia, <1967[25]	Residual sera	207 (5)	HAI-?	A	194 (101,774)	82 (0,1000)	81 (71,100)	46 (0,119)	0.9 (2)	51	D	C
				B	117 (89,140)	6 (0,40)	--	27 (0,131)	1.7 (3)	31		
				C	207 (122,790)	207 (122,790)	79 (70,88)	33 (0,112)	1 (3)	31		
				D	75 (61,92)	75 (61,92)	--	203 (167,234)	16.2 (4)	39		
China, 1979-80[67]	Residual sera	16658 (11)	HAI-?	A	295 (283,311)	2 (0,24)	98 (97,99)	1 (0,8)	134.2 (8)	217	A	D
				B	268 (262,275)	0 (0,0)	--	0 (0,0)	153.1 (9)	232		
				C	318 (306,330)	318 (306,330)	96 (96,97)	7 (5,8)	150.5 (9)	229		
				D	205 (199,212)	205 (199,212)	--	34 (31,37)	1332.3 (10)	1408		
Fiji, <1973[60]	Sera from F in all ages	1174 (9)	HAI-1:4	A	29 (23,35)	81 (63,120)	97 (92,100)	364 (332,391)	62.1 (6)	108	C	D
				B	29 (24,35)	68 (59,81)	--	356 (325,387)	64.6 (7)	105		
				C	45 (42,49)	45 (42,49)	100 (100,100)	260 (255,262)	93 (7)	134		
				D	45 (42,49)	45 (42,49)	--	260 (255,262)	93 (8)	130		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Japan (Sapporo), <1967[25]	Residual sera	188 (5)	HAI-?	A	1000 (109,1000)	820 (0,1000)	50 (44,62)	0 (0,18)	15.6 (2)	65	D	D
				B	62 (50,75)	0 (0,0)	--	0 (0,0)	19.6 (3)	49		
				C	1000 (174,1000)	1000 (174,1000)	50 (44,59)	0 (0,53)	15.6 (3)	45		
				D	34 (27,41)	34 (27,41)	--	262 (253,264)	47.3 (4)	70		
Japan (Ohtsu), <1967[25]	Residual sera	155 (5)	HAI-?	A	47 (8,98)	171 (2,1000)	38 (28,100)	262 (13,417)	0.1 (2)	48	B	D
				B	18 (6,32)	15 (0,31)	--	187 (0,345)	0.5 (3)	28		
				C	28 (13,128)	28 (13,128)	66 (29,100)	255 (103,264)	0.5 (3)	28		
				D	16 (12,22)	16 (12,22)	--	206 (168,235)	0.6 (4)	21		
Malaysia, <1972[61]	F hospital patients, pregnant F	697 (6)	HAI-1:10	A	54 (42,1000)	22 (14,39)	100 (62,100)	159 (0,225)	22.8 (3)	70	B	B
				B	54 (42,66)	22 (12,32)	--	159 (91,225)	22.8 (4)	60		
				C	51 (35,1000)	51 (35,1000)	86 (59,100)	252 (0,264)	30.1 (4)	67		
				D	38 (34,42)	38 (34,42)	--	264 (262,264)	30.9 (5)	63		
Singapore, 1975-79[62]	Pregnant women and F (child-bearing age)	2284 (5)	HAI-1:8	A	13 (0,89)	244 (106,364)	55 (52,60)	345 (156,447)	4.7 (2)	65	B	C
				B	47 (35,58)	11 (1,22)	--	105 (10,197)	10.7 (3)	51		
				C	86 (54,145)	86 (54,145)	59 (53,70)	179 (82,248)	7.9 (3)	49		
				D	28 (27,30)	28 (27,30)	--	255 (252,258)	22 (4)	56		

Country, year of study, reference	Study population	Sample size (no. of age groups)	Lab test (cut-off)	Cata-lytic model	Force of infection (/1000/year)		Sensitivity (%)	CRS/ 100,000 live births	Loglike-lihood deviance (deg of freedom)	AICc	Selected model according to criterion:	
					<13 yr olds	≥13 yr olds					1	2
Taiwan, 1984[63]	F on maternity ward	154 (5)	HAI:1-8	A	90 (0,442)	68 (0,674)	100 (85,100)	167 (0,471)	0.5 (2)	43	B	D
				B	90 (0,176)	68 (0,161)	--	167 (0,475)	0.5 (3)	23		
				C	79 (67,984)	79 (67,984)	100 (84,100)	195 (0,221)	0.6 (3)	23		
				D	79 (66,97)	79 (66,97)	--	195 (156,224)	0.6 (4)	16		
Taiwan, 1984-6[64]	Sera from older girls and women of child-bearing age	2030 (4)	HAI	A	122 (99,150)	756 (390,1000)	62 (59,66)	30 (14,70)	5.5 (1)	-	B	D
				B	62 (56,68)	28 (10,47)	--	168 (72,227)	12.1 (2)	55		
				C	102 (70,140)	102 (70,140)	72 (64,88)	147 (87,216)	11.8 (2)	54		
				D	55 (52,58)	55 (52,58)	--	246 (239,251)	20 (3)	51		

Notes: See Table H for the definitions of the abbreviations.

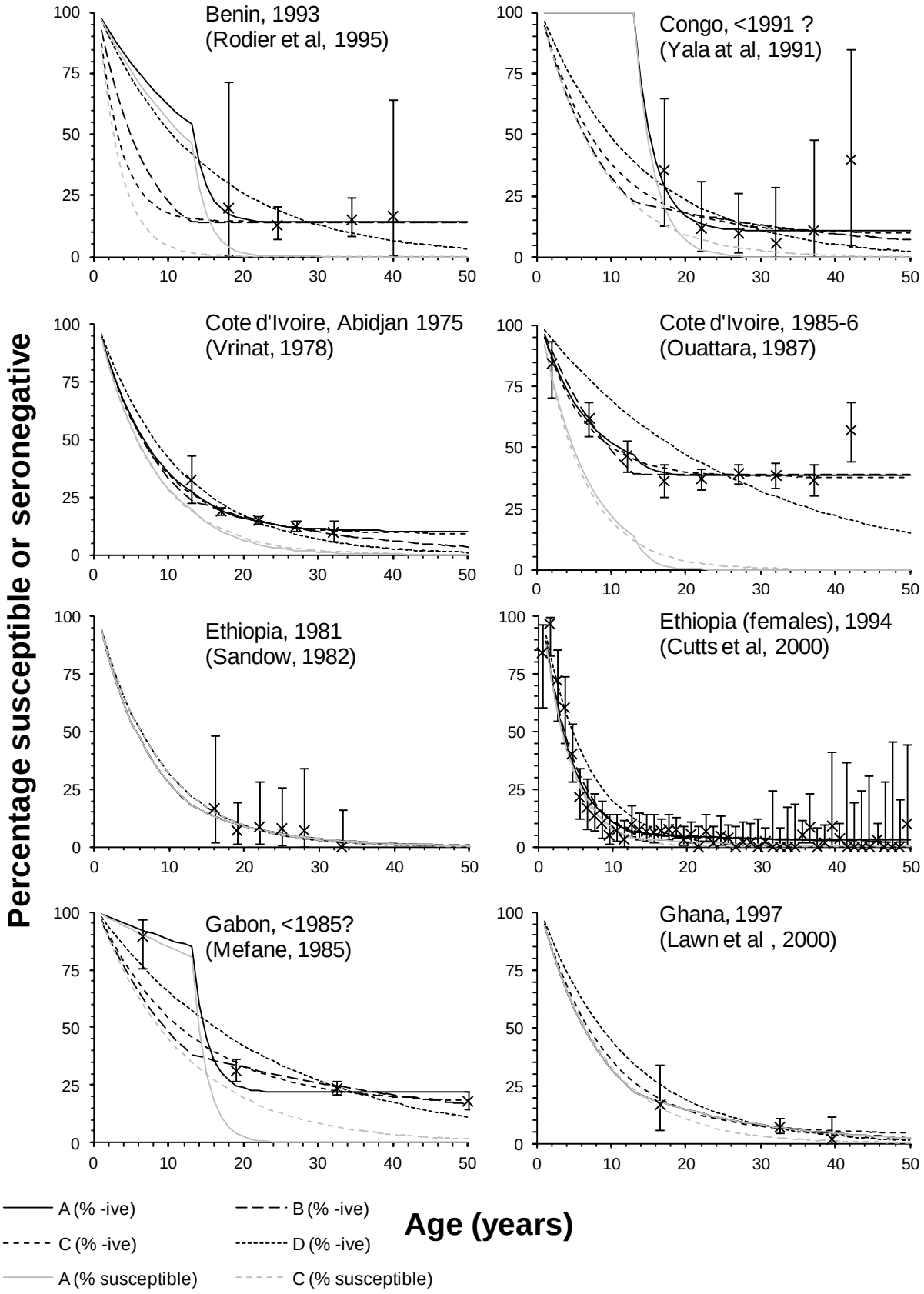

Figure Ba: Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed in different settings in the African WHO region. The crosses show the observed percentage seronegative together with 95% (exact) confidence intervals

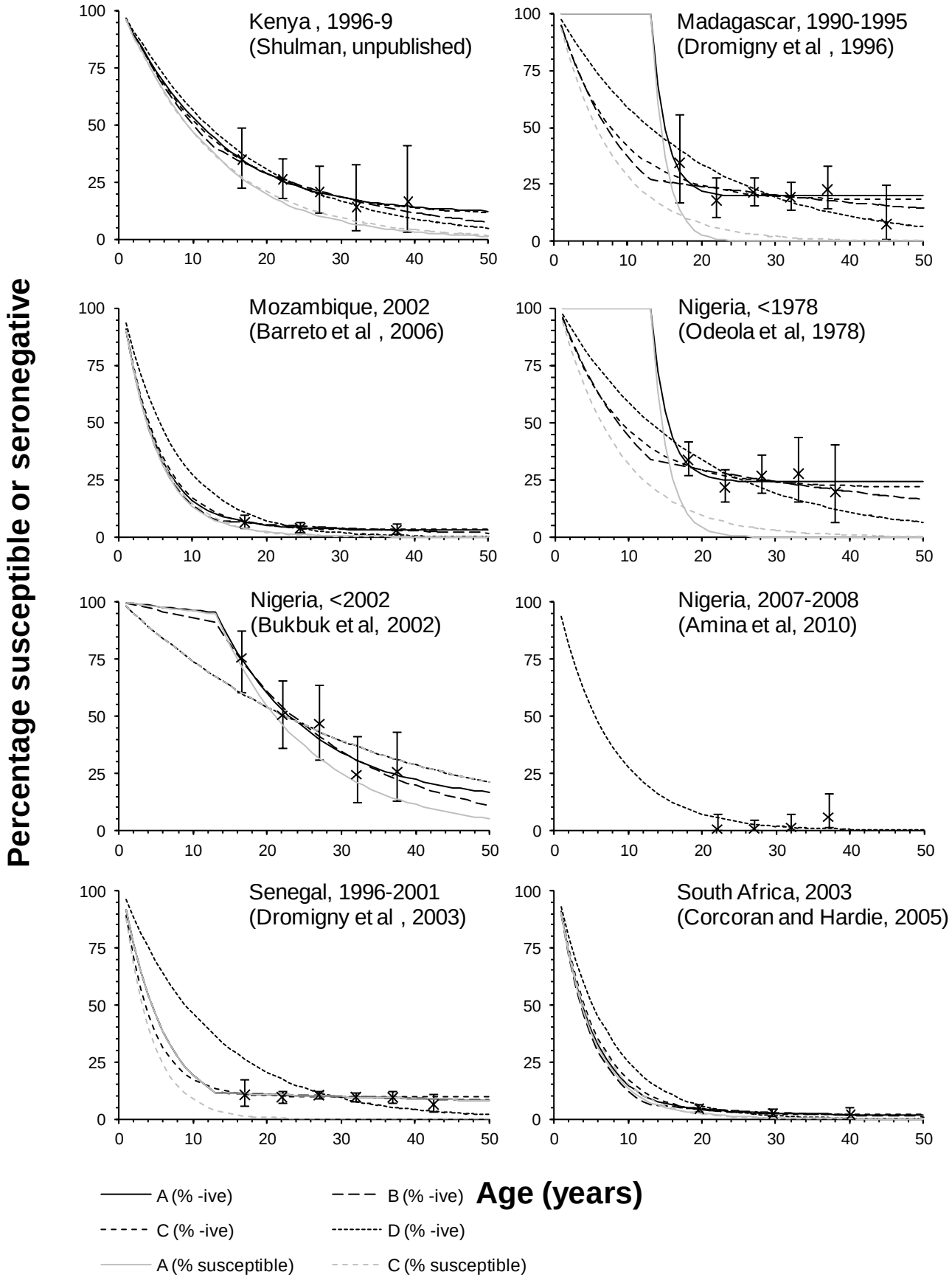

Figure Bb: Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed in different settings in the African WHO region. The crosses show the observed percentage seronegative together with 95% (exact) confidence intervals.

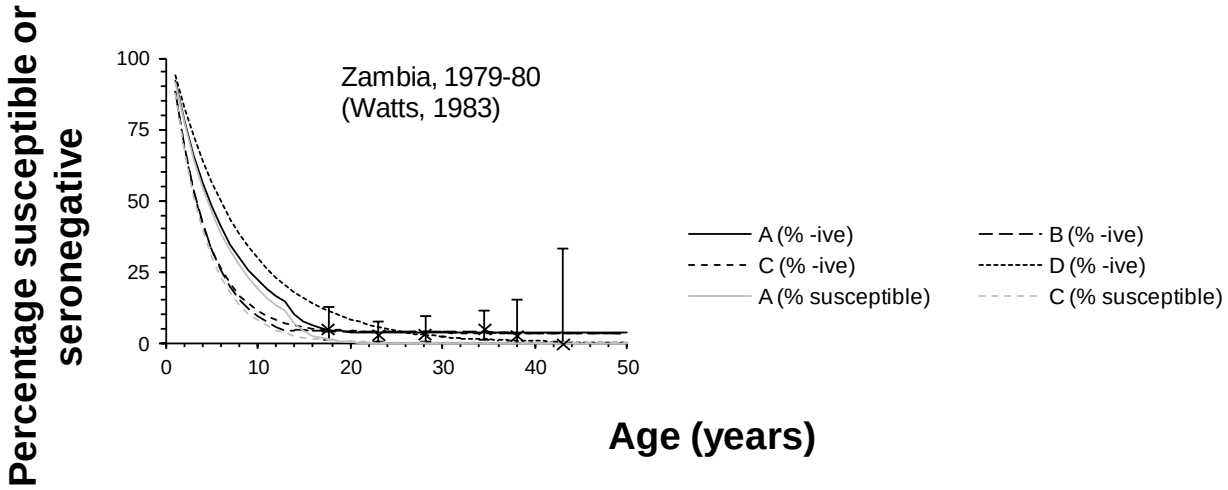

Figure Bc: Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed in different settings in the African WHO region. The crosses show the observed percentage seronegative together with 95% (exact) confidence intervals.

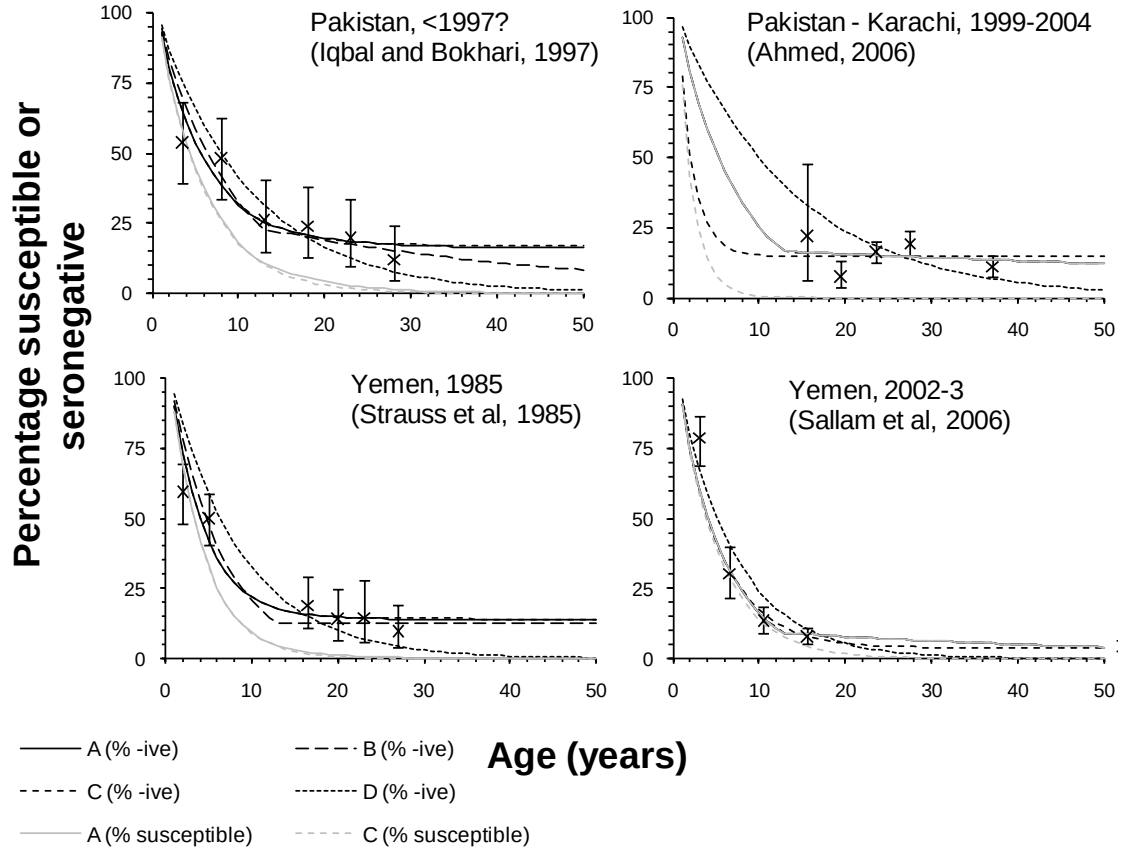

Figure C: Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed in different settings in the Eastern Mediterranean WHO region. The crosses show the observed percentage seronegative together with 95% (exact) confidence intervals.

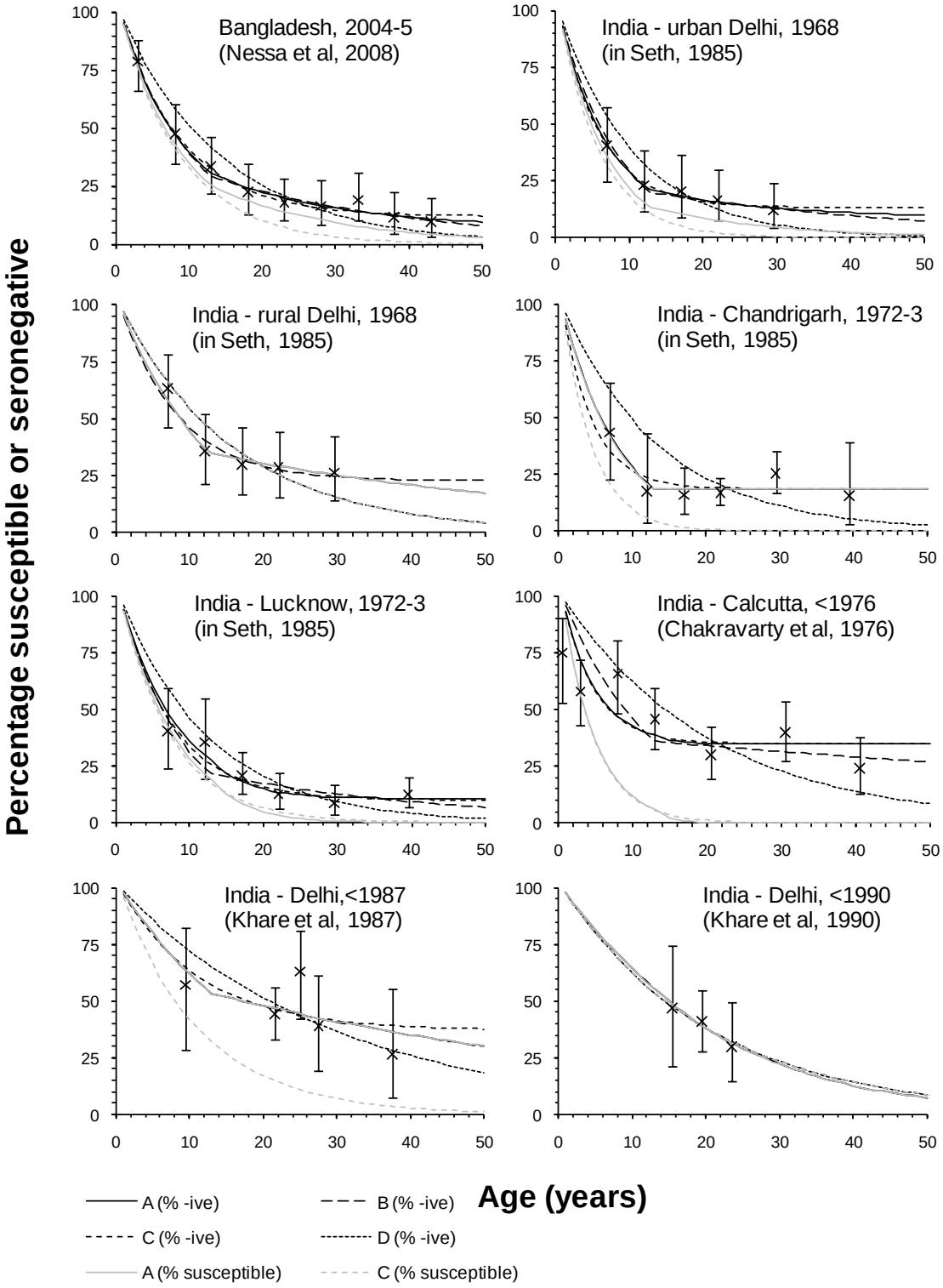

Figure Da: Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed in different settings in the South East Asian WHO region. The crosses show the observed percentage seronegative, together with 95% (exact) confidence intervals.

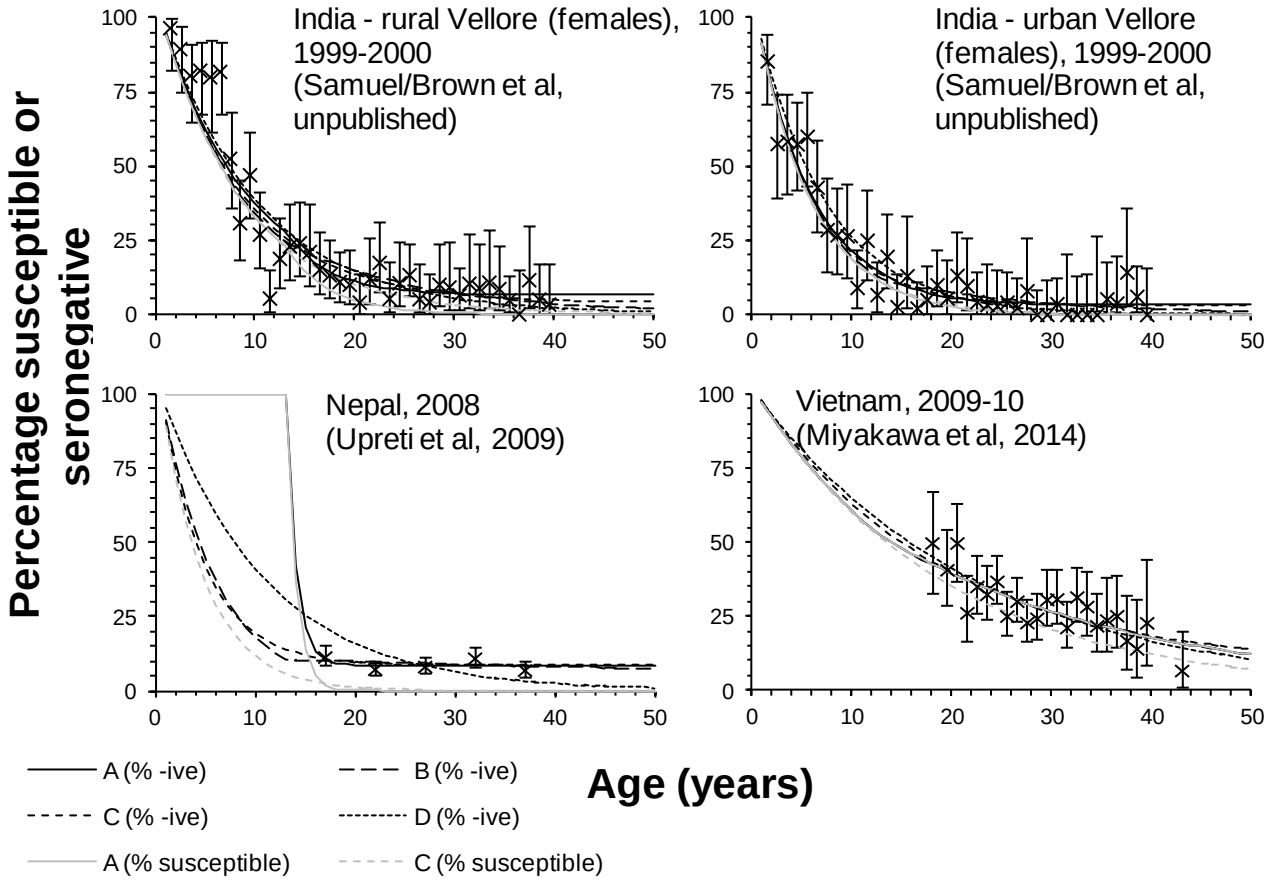

Figure Db: Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed in different settings in the South East Asian and Western Pacific regions. The crosses show the observed percentage seronegative together with 95% (exact) confidence intervals.

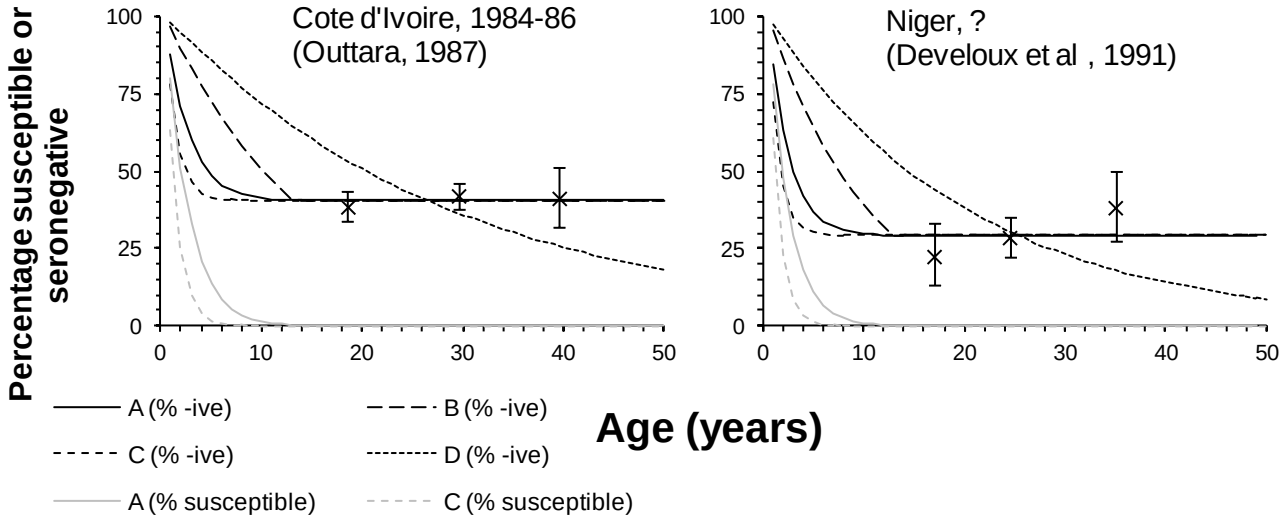

Figure E: Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed for the two datasets for which the selected catalytic models fitted poorly. The crosses show the observed percentage seronegative, together with 95% (exact) confidence intervals.

E: Estimates of the CRS incidence

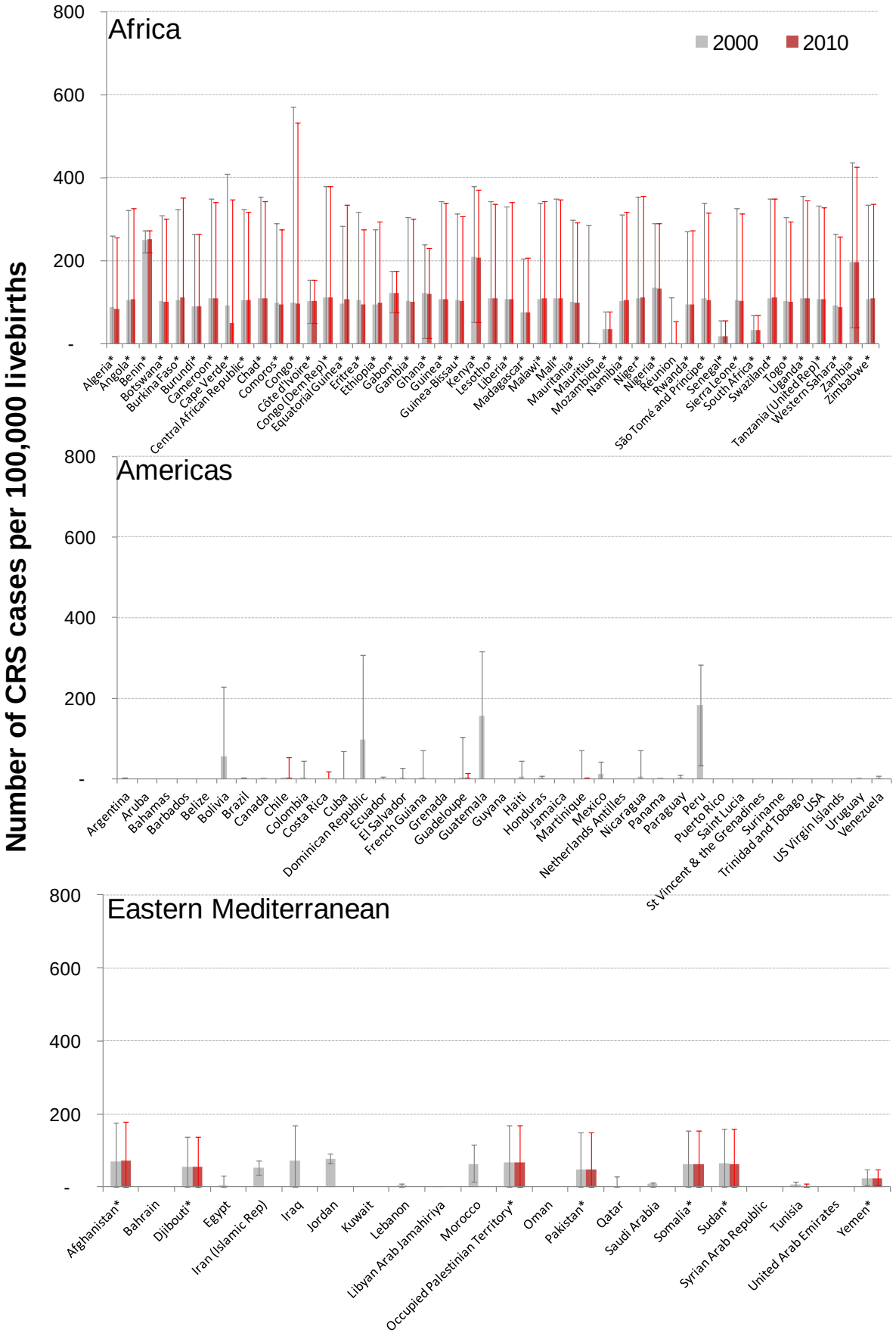

Figure Fa: Estimates of the incidence of CRS per 100,000 live births among 15-44 year olds in the African, American and Eastern Mediterranean WHO Regions in 2000 and 2010. Countries in which rubella vaccination had not been introduced by the year 2010 (either into the routine schedule or during a campaign) are indicated using an asterisk.

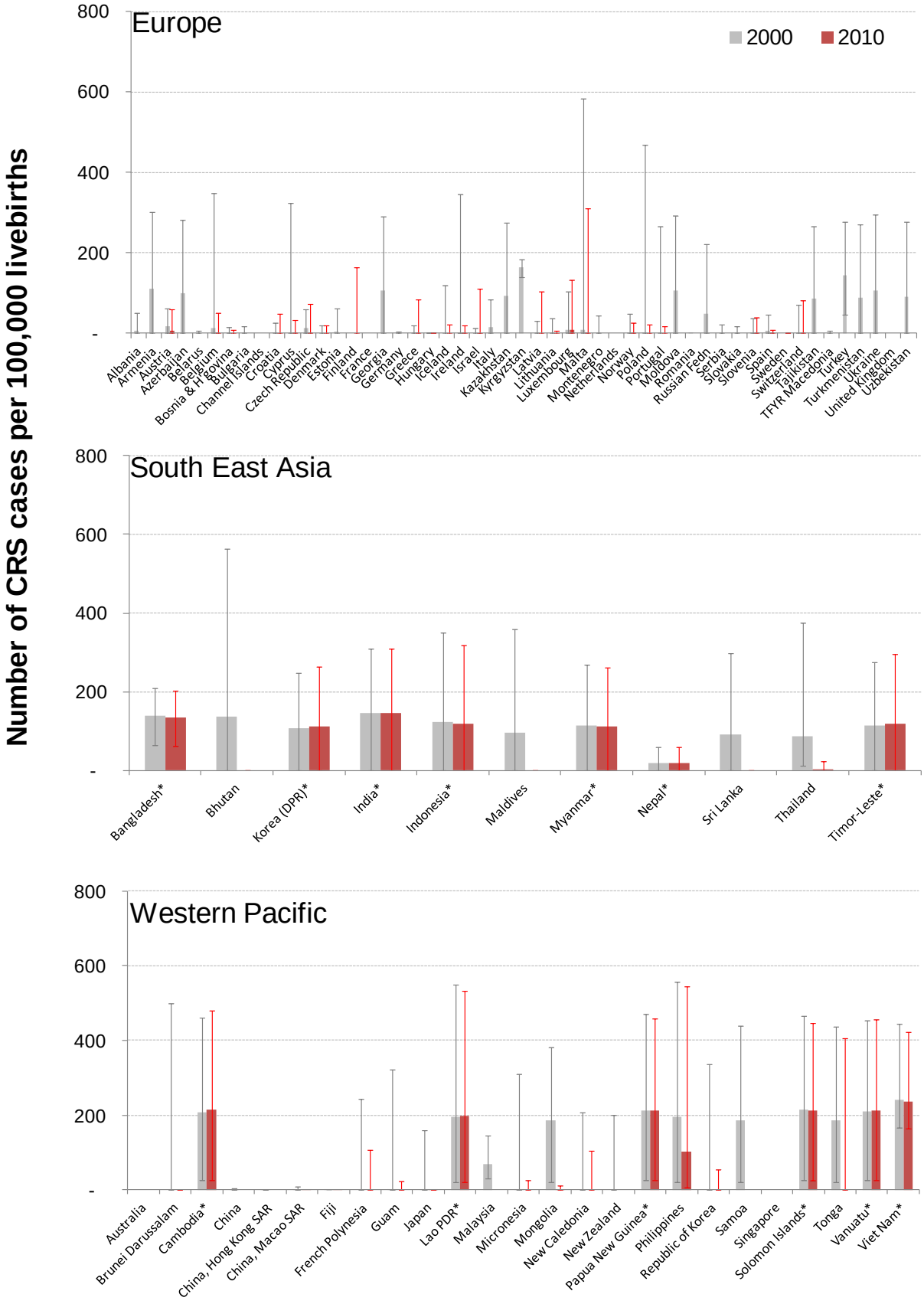

Figure Fb: Estimates of the incidence of CRS per 100,000 live births among 15-44 year olds in the European, South East Asian and Western Pacific WHO Regions in 2000 and 2010. Countries in which rubella vaccination had not been introduced by the year 2010 (either into the routine schedule or during a campaign) are indicated using an asterisk.

Table J: Estimated numbers of CRS cases per 100,000 live births and overall number by WHO region and year. The different columns reflect estimates obtained by using datasets for countries based on WHO/geographical region or GBD regions for settings which did not have serological datasets predating the introduction of RCV. The values in parentheses reflect the values at the lowest and highest limits of the 95% CI. The reduction in the burden in CRS between the years 2004 and 2005 is attributable to a change in the value for the fertility rate that is used in these calculations, which uses the average value for the period 2000-2004 for each year in this period and the average value for the period 2005-2010 for each year in subsequent years.

Region	Year	WHO grouping		GBD grouping	
		CRS incidence per 100,000 live births	Total number of CRS cases	CRS incidence per 100,000 live births	Total number of CRS cases
AFRO	1996	115 (55,231)	28315 (13443,57421)	121 (74,181)	29976 (18488,46525)
	2000	116 (55,232)	30464 (14411,61846)	121 (74,182)	32317 (19812,50053)
	2001	116 (55,233)	31388 (14829,63821)	121 (74,182)	33313 (20403,51690)
	2002	116 (55,233)	32354 (15256,65870)	122 (74,183)	34350 (21021,53415)
	2003	116 (55,234)	33344 (15690,67970)	122 (74,183)	35400 (21638,55161)
	2004	116 (55,234)	34355 (16132,70130)	122 (74,184)	36475 (22269,56946)
	2005	116 (56,235)	33696 (15813,68886)	122 (74,184)	35770 (21574,55277)
	2006	116 (56,235)	34682 (16250,71023)	122 (74,185)	36817 (22196,57039)
	2007	116 (56,235)	35662 (16695,73202)	122 (74,185)	37891 (22834,58836)
	2008	116 (56,235)	36657 (17146,75411)	122 (74,185)	38982 (23486,60661)
	2009	116 (56,235)	37675 (17603,77635)	122 (74,186)	40090 (24164,62438)
	2010	116 (56,235)	38712 (18063,79852)	122 (74,186)	41194 (24844,64198)
AMRO	1996	56 (24,104)	10640 (4394,19867)	68 (34,105)	13337 (6730,20302)
	2000	11 (6,23)	2514 (1160,4990)	12 (7,23)	2633 (1379,5017)
	2001	6 (1,17)	1164 (276,3092)	6 (2,12)	1369 (567,2714)
	2002	2 (0,13)	541 (8,2623)	3 (0,7)	685 (73,1434)
	2003	2 (0,21)	421 (1,4117)	2 (0,11)	464 (18,2166)
	2004	1 (0,24)	168 (0,4586)	1 (0,12)	153 (4,2303)
	2005	<1 (0,1)	25 (0,170)	<1 (0,1)	12 (1,99)
	2006	<0.1 (0,2)	4 (0,187)	<0.1 (0,0.2)	1 (0,34)
	2007	<0.01 (0,1)	1 (0,62)	<0.1 (0,0.2)	1 (0,30)
	2008	<0.01 (0,1)	1 (0,94)	<0.01 (0,1)	<1 (0,93)
	2009	<0.01 (0,1)	<1 (0,198)	<0.01 (0,1)	<1 (0,198)
	2010	<0.01 (0,1)	<1 (0,136)	<0.01 (0,1)	<1 (0,136)
EMRO	1996	56 (22,106)	7625 (2577,15290)	62 (31,105)	8708 (4078,14945)
	2000	42 (16,82)	6216 (1927,12580)	47 (23,83)	6874 (3036,12708)
	2001	39 (15,77)	5933 (1830,12202)	43 (21,79)	6606 (2832,12672)
	2002	37 (15,74)	5882 (1794,12088)	41 (19,77)	6480 (2744,12713)
	2003	30 (8,67)	5336 (1217,11607)	34 (13,72)	5934 (2092,12423)
	2004	27 (6,63)	5033 (977,11393)	31 (10,67)	5658 (1750,12134)
	2005	26 (5,62)	4609 (839,10652)	30 (9,65)	5209 (1508,11301)
	2006	26 (4,61)	4719 (748,10985)	29 (8,65)	5330 (1489,11620)
	2007	26 (4,61)	4828 (756,11297)	29 (7,65)	5419 (1508,11974)
	2008	25 (4,61)	4977 (776,11643)	29 (7,65)	5586 (1539,12350)
	2009	25 (4,61)	5133 (799,12000)	29 (7,65)	5762 (1586,12732)
	2010	25 (4,61)	5294 (827,12358)	29 (7,65)	5938 (1639,13115)

Region	Year	WHO grouping		GBD grouping	
		CRS incidence per 100,000 live births	Total number of CRS cases	CRS incidence per 100,000 live births	Total number of CRS cases
EURO	1996	65 (14,133)	8155 (1839,15349)	108 (99,130)	11217 (9596,14211)
	2000	45 (6,114)	6004 (1030,13266)	79 (70,97)	8493 (7089,11075)
	2001	31 (5,86)	4811 (877,10942)	51 (39,71)	6176 (4554,9067)
	2002	25 (6,73)	4315 (900,9991)	37 (20,60)	5073 (3076,8221)
	2003	23 (5,68)	4167 (887,9558)	34 (16,57)	4737 (2651,7942)
	2004	21 (5,57)	3830 (845,8488)	26 (12,48)	4030 (2291,7020)
	2005	20 (5,46)	3421 (762,7039)	20 (11,40)	3304 (1902,6043)
	2006	9 (2,28)	1483 (275,4216)	9 (4,28)	1406 (738,4010)
	2007	4 (0,17)	629 (32,2247)	3 (2,15)	528 (336,2018)
	2008	3 (0,13)	415 (3,1578)	2 (1,9)	434 (311,1098)
	2009	1 (0,6)	179 (2,651)	1 (0,6)	108 (49,597)
	2010	1 (0,5)	98 (1,507)	1 (0,6)	74 (9,525)
SEARO	1996	130 (43,251)	50128 (14587,96435)	153 (52,261)	57718 (17649,100090)
	2000	126 (39,246)	48252 (13196,93822)	149 (48,258)	55585 (16228,97150)
	2001	127 (40,250)	49121 (13747,95800)	149 (51,259)	56522 (17160,99344)
	2002	126 (39,248)	49995 (13706,97141)	148 (49,257)	57204 (16666,100990)
	2003	126 (38,245)	50863 (14028,98629)	147 (48,256)	57804 (16938,102631)
	2004	127 (38,248)	51836 (13800,100761)	148 (49,257)	58868 (17433,104390)
	2005	126 (38,245)	46997 (12609,91745)	147 (46,256)	53485 (15253,94892)
	2006	123 (34,241)	47136 (11421,92047)	144 (40,251)	53723 (14036,95305)
	2007	122 (31,239)	47470 (11155,92973)	143 (39,250)	54225 (13797,96543)
	2008	121 (31,238)	47963 (11201,94307)	142 (39,250)	54861 (13937,97824)
	2009	121 (31,238)	48613 (11189,95655)	141 (39,250)	55514 (13977,99185)
	2010	121 (31,238)	49229 (11204,96976)	141 (38,250)	56166 (14144,100485)
WPRO (excluding China)	1996	118 (58,225)	11368 (5137,21938)	118 (71,222)	11424 (6949,22046)
	2000	117 (60,206)	10922 (5020,20115)	125 (74,222)	11182 (6882,21587)
	2001	117 (59,207)	11037 (5048,20484)	123 (72,223)	11162 (6677,21948)
	2002	116 (59,213)	11086 (5072,21173)	120 (74,223)	11329 (7064,22414)
	2003	114 (58,221)	11215 (5169,21917)	118 (71,223)	11363 (6785,22762)
	2004	113 (58,221)	11420 (5126,22150)	118 (73,223)	11595 (7121,23306)
	2005	111 (57,209)	10551 (4698,20424)	114 (70,219)	10643 (6233,21522)
	2006	109 (54,203)	10510 (4552,20359)	112 (69,218)	10606 (6467,21711)
	2007	109 (53,200)	10569 (4509,20480)	110 (66,216)	10627 (6070,21903)
	2008	109 (53,196)	10689 (4522,20676)	111 (68,215)	10783 (6481,22219)
	2009	107 (52,195)	10658 (4529,20884)	108 (63,213)	10692 (6012,22393)
	2010	90 (46,195)	8889 (4010,21118)	91 (54,213)	8833 (5184,22681)
WPRO (including China)	1996	30 (15,55)	11541 (5268,21980)	29 (18,55)	11645 (7095,22325)
	2000	30 (15,52)	11084 (5328,20167)	32 (19,56)	11381 (7035,21802)
	2001	30 (15,53)	11163 (5372,20599)	31 (18,56)	11393 (6858,22063)
	2002	29 (15,54)	11242 (5300,21277)	31 (19,56)	11536 (7149,22634)
	2003	29 (15,56)	11392 (5284,21940)	30 (18,56)	11579 (6966,22962)
	2004	29 (15,56)	11565 (5290,22339)	30 (19,57)	11827 (7240,23515)
	2005	29 (15,53)	10710 (4839,20583)	29 (18,56)	10845 (6414,21679)
	2006	28 (14,52)	10684 (4635,20590)	29 (18,56)	10835 (6584,21873)
	2007	28 (14,51)	10774 (4611,20595)	29 (17,55)	10835 (6236,22113)
	2008	28 (14,50)	10725 (4573,20722)	28 (17,55)	10851 (6520,22255)
	2009	27 (13,50)	10660 (4529,20884)	28 (16,55)	10694 (6013,22394)
	2010	23 (12,50)	8889 (4010,21118)	23 (14,55)	8833 (5184,22681)

Region	Year	WHO grouping		GBD grouping	
		CRS incidence per 100,000 live births	Total number of CRS cases	CRS incidence per 100,000 live births	Total number of CRS cases
Global	1996	--	119224 (72119,169107)	--	133422 (88796,177332)
	2000		107156 (62121,154446)		118331 (75525,163652)
	2001		106508 (60618,155183)		116460 (71977,163067)
	2002		107408 (59964,157276)		116122 (71314,162864)
	2003		108854 (60061,159270)		116664 (70544,164815)
	2004		110271 (60553,162017)		118115 (71916,167908)
	2005		101841 (55603,149394)		109399 (66099,154955)
	2006		101778 (54629,150035)		108948 (65034,155067)
	2007		102304 (53638,152542)		109643 (63325,156382)
	2008		103845 (54373,156443)		111570 (65732,160816)
	2009		105212 (55087,158598)		112499 (64267,162105)
	2010		105391 (53605,158041)		113254 (65649,162674)

F: Sensitivity analyses

6.1 The effect of selective vaccination coverage

Table K: Estimates of the regional and global numbers of CRS cases predicted to have been born each year during 1996-2010, assuming that the selective vaccination coverage in countries which had introduced selective vaccination of adolescents was either 50% (medium, as in the base-case model), 10% (low) or 90% (high). The numbers in parentheses reflect the 95% CI, obtained by bootstrapping.

Region	Year	Numbers of CRS cases assuming a vaccination coverage among adolescents of:		
		50% (Medium)	**10% (Low)**	**90% (High)**
AFRO	1996	28315 (13443,57421)	28316 (13443,57431)	28315 (13443,57411)
	2000	30464 (14411,61846)	30465 (14411,61856)	30461 (14411,61834)
	2001	31388 (14829,63821)	31391 (14829,63826)	31386 (14829,63807)
	2002	32354 (15256,65870)	32359 (15256,65871)	32353 (15256,65857)
	2003	33344 (15690,67970)	33348 (15690,67972)	33343 (15690,67961)
	2004	34355 (16132,70130)	34358 (16132,70133)	34354 (16132,70125)
	2005	33696 (15813,68886)	33698 (15813,68890)	33695 (15813,68884)
	2006	34682 (16250,71023)	34683 (16250,71029)	34681 (16250,71021)
	2007	35662 (16695,73202)	35663 (16695,73209)	35662 (16695,73199)
	2008	36657 (17146,75411)	36657 (17146,75419)	36657 (17146,75407)
	2009	37675 (17603,77635)	37675 (17603,77639)	37675 (17603,77629)
	2010	38712 (18063,79852)	38712 (18063,79854)	38712 (18063,79848)
AMRO	1996	10640 (4394,19867)	11341 (4483,21577)	9973 (4240,18225)
	2000	2514 (1160,4990)	2767 (1166,5065)	2470 (1146,4960)
	2001	1164 (276,3092)	1193 (276,2897)	1162 (276,2835)
	2002	541 (8,2623)	550 (8,2670)	533 (8,2584)
	2003	421 (1,4117)	434 (1,4112)	418 (1,4102)
	2004	168 (0,4586)	171 (0,4586)	168 (0,4579)
	2005	25 (0,170)	26 (0,284)	17 (0,130)
	2006	4 (0,187)	4 (0,167)	1 (0,34)
	2007	1 (0,62)	2 (0,69)	1 (0,32)
	2008	1 (0,94)	2 (0,96)	<1 (0,93)
	2009	<1 (0,198)	1 (0,200)	<1 (0,198)
	2010	<1 (0,136)	2 (0,136)	<1 (0,136)
EMRO	1996	7625 (2577,15290)	7716 (2634,15479)	7545 (2526,15166)
	2000	6216 (1927,12580)	6290 (1986,12719)	6106 (1871,12444)
	2001	5933 (1830,12202)	6085 (1880,12373)	5845 (1776,12045)
	2002	5882 (1794,12088)	6019 (1905,12298)	5730 (1688,11890)
	2003	5336 (1217,11607)	5425 (1249,11752)	5274 (1206,11474)
	2004	5033 (977,11393)	5047 (980,11414)	5030 (973,11374)
	2005	4609 (839,10652)	4610 (839,10652)	4607 (838,10652)
	2006	4719 (748,10985)	4720 (749,10985)	4719 (747,10984)
	2007	4828 (756,11297)	4828 (757,11297)	4828 (756,11297)
	2008	4977 (776,11643)	4978 (776,11643)	4977 (776,11643)
	2009	5133 (799,12000)	5133 (799,12001)	5133 (799,12000)
	2010	5294 (827,12358)	5294 (827,12359)	5294 (826,12358)

Region	Year	Numbers of CRS cases assuming a vaccination coverage among adolescents of:		
		50% (Medium)	**10% (Low)**	**90% (High)**
EURO	1996	8155 (1839,15349)	8401 (1869,17772)	8006 (1818,14875)
	2000	6004 (1030,13266)	6241 (1152,13394)	5871 (997,12048)
	2001	4811 (877,10942)	5046 (941,10712)	4641 (833,9945)
	2002	4315 (900,9991)	4563 (875,9500)	4193 (825,9045)
	2003	4167 (887,9558)	4420 (863,8986)	4034 (825,8651)
	2004	3830 (845,8488)	4018 (864,8004)	3760 (817,7782)
	2005	3421 (762,7039)	3587 (786,6703)	3323 (777,6737)
	2006	1483 (275,4216)	1836 (299,4404)	1381 (286,4109)
	2007	629 (32,2247)	920 (34,2849)	440 (40,2178)
	2008	415 (3,1578)	459 (3,2151)	350 (4,1494)
	2009	179 (2,651)	271 (2,1058)	96 (1,531)
	2010	98 (1,507)	229 (1,741)	47 (0,406)
SEARO	1996	50128 (14587,96435)	50888 (15063,97234)	49479 (13379,95830)
	2000	48252 (13196,93822)	48654 (13658,94485)	47639 (12523,93091)
	2001	49121 (13747,95800)	49360 (14200,95973)	48930 (13265,95331)
	2002	49995 (13706,97141)	50137 (13796,97533)	49760 (13436,96958)
	2003	50863 (14028,98629)	50936 (14333,99045)	50525 (13274,98520)
	2004	51836 (13800,100761)	51994 (13907,100812)	51568 (13659,100321)
	2005	46997 (12609,91745)	47029 (12922,92003)	46912 (12176,91697)
	2006	47136 (11421,92047)	47185 (11478,92055)	46999 (11377,92003)
	2007	47470 (11155,92973)	47504 (11184,92990)	47429 (11132,92948)
	2008	47963 (11201,94307)	48018 (11278,94308)	48013 (11163,94302)
	2009	48613 (11189,95655)	48613 (11238,95653)	48622 (11169,95652)
	2010	49229 (11204,96976)	49230 (11184,96958)	49210 (11318,96972)
WPRO	1996	11368 (5137,21938)	12163 (5862,22339)	11278 (5064,21357)
	2000	10922 (5020,20115)	11612 (5659,20834)	10652 (4766,19729)
	2001	11037 (5048,20484)	11766 (5704,21343)	10808 (4810,20332)
	2002	11086 (5072,21173)	11962 (5702,22005)	10957 (4897,20913)
	2003	11215 (5169,21917)	12143 (5822,22915)	11122 (4986,21807)
	2004	11420 (5126,22150)	12438 (5815,22958)	11290 (5023,21995)
	2005	10551 (4698,20424)	11511 (5294,21017)	10506 (4619,20302)
	2006	10510 (4552,20359)	11347 (4872,20670)	10617 (4601,20396)
	2007	10569 (4509,20480)	11263 (4706,20676)	10760 (4605,20543)
	2008	10689 (4522,20676)	11152 (4628,20784)	10724 (4573,20688)
	2009	10658 (4529,20884)	10892 (4596,20914)	10658 (4529,20869)
	2010	8889 (4010,21118)	9088 (4218,21162)	8889 (4010,21111)
Global	1996	119224 (72119,169107)	122125 (74616,171420)	116953 (70207,166391)
	2000	107156 (62121,154446)	109017 (63871,156852)	105685 (60576,152003)
	2001	106508 (60618,155183)	107715 (61755,156833)	105219 (58909,153593)
	2002	107408 (59964,157276)	108852 (61880,158470)	106140 (58333,155819)
	2003	108854 (60061,159270)	110394 (61227,160682)	107768 (59085,157527)
	2004	110271 (60553,162017)	111897 (61532,163543)	109193 (59756,161058)
	2005	101841 (55603,149394)	103489 (56688,150935)	101314 (55561,148732)
	2006	101778 (54629,150035)	102628 (55585,152081)	101432 (54060,149950)
	2007	102304 (53638,152542)	102750 (54054,153444)	102099 (53350,152856)
	2008	103845 (54373,156443)	104336 (54673,157511)	103691 (54220,155507)
	2009	105212 (55087,158598)	105617 (55181,158917)	105107 (54870,158344)
	2010	105391 (53605,158041)	105838 (53898,158994)	105232 (53404,158782)

6.2 The effect of including additional datasets

Table L: Estimates of the numbers of CRS cases in the African region and globally predicted to have been born each year during 1996-2010, obtained in the base-case and after including the two datasets (from Niger[98] and Cote D'Ivoire[97]) which had been dropped due to the poor fit of the catalytic models to the data. The numbers in parentheses reflect the 95% CI, obtained by bootstrapping.

	Excluding datasets from Niger[98] and Cote d'Ivoire[97] (base case)		Including datasets from Niger[98] and Cote d'Ivoire[97]	
Year	**CRS incidence per 100,000 live births**	**Numbers of CRS cases**	**CRS incidence per 100,000 live births**	**Numbers of CRS cases**
Africa				
1996	115 (55,231)	28315 (13443,57421)	124 (63,236)	30700 (15088,58648)
2000	116 (55,232)	30464 (14411,61846)	125 (63,237)	33130 (16316,63022)
2001	116 (55,233)	31388 (14829,63821)	125 (63,237)	34149 (16800,65002)
2002	116 (55,233)	32354 (15256,65870)	125 (63,238)	35195 (17297,67049)
2003	116 (55,234)	33344 (15690,67970)	125 (63,238)	36266 (17807,69117)
2004	116 (55,234)	34355 (16132,70130)	126 (63,238)	37357 (18328,71246)
2005	116 (56,235)	33696 (15813,68886)	126 (64,240)	36812 (18281,69954)
2006	116 (56,235)	34682 (16250,71023)	126 (64,240)	37888 (18823,72041)
2007	116 (56,235)	35662 (16695,73202)	126 (64,240)	39003 (19378,74135)
2008	116 (56,235)	36657 (17146,75411)	126 (64,240)	40127 (19945,76317)
2009	116 (56,235)	37675 (17603,77635)	126 (64,240)	41292 (20521,78541)
2010	116 (56,235)	38712 (18063,79852)	126 (64,240)	42460 (21105,80779)
Global				
1996		119224 (72119,169107)		120550 (75072,176115)
2000		107156 (62121,154446)		108757 (65399,158754)
2001		106508 (60618,155183)		108294 (63718,158788)
2002		107408 (59964,157276)		109286 (64244,160594)
2003		108854 (60061,159270)		110608 (64466,162564)
2004		110271 (60553,162017)		112733 (65479,165188)
2005		101841 (55603,149394)		104316 (60937,154006)
2006		101778 (54629,150035)		104074 (58460,154410)
2007		102304 (53638,152542)		104546 (57755,157104)
2008		103845 (54373,156443)		106434 (57756,161225)
2009		105212 (55087,158598)		107566 (58392,163190)
2010		105391 (53605,158041)		107866 (57565,163342)

6.3 Effect of excluding individual datasets

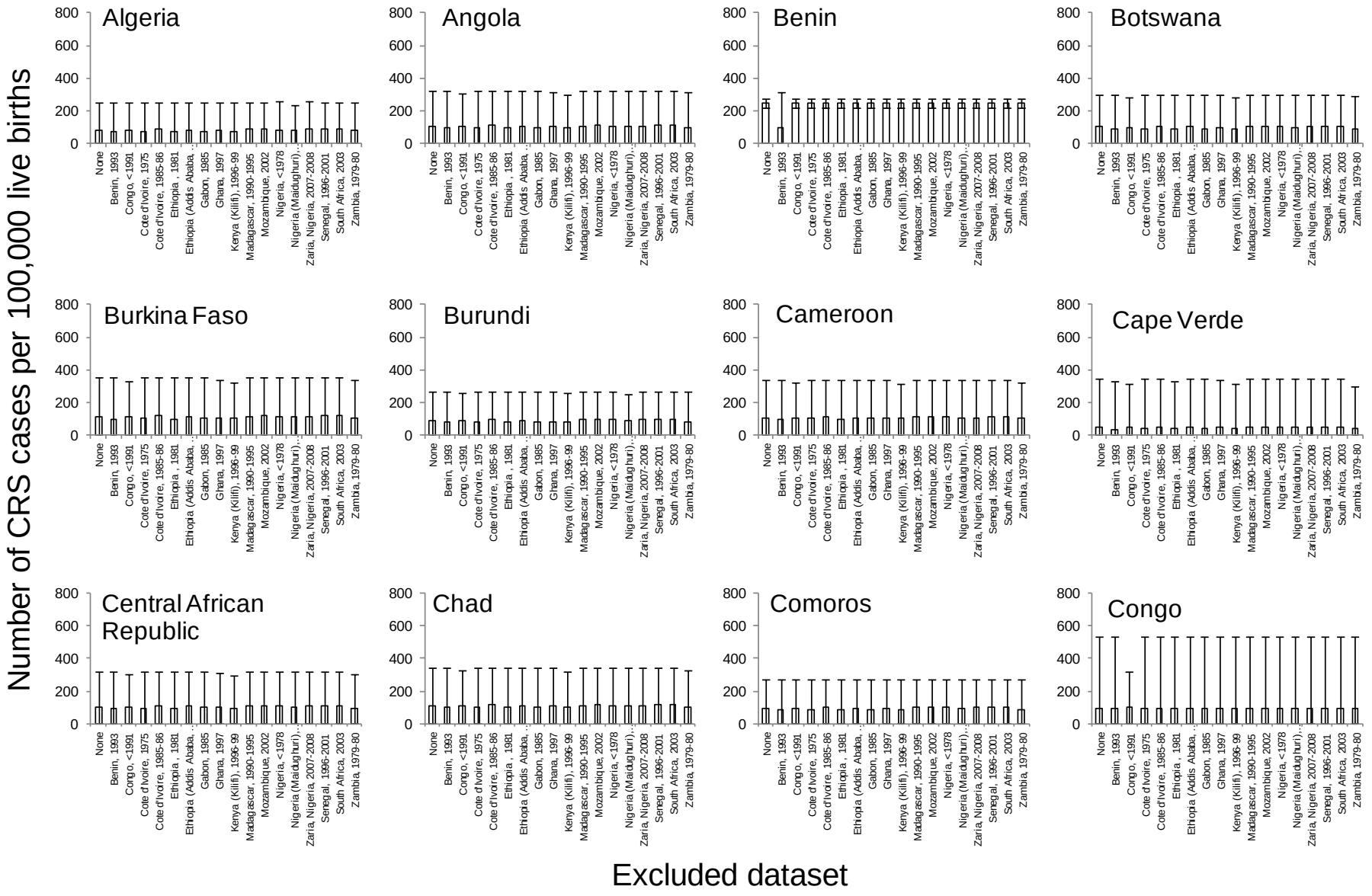

Figure G: Estimates of the country-specific CRS incidence per 100,000 live births in Africa in 2010, calculated after excluding individual datasets.

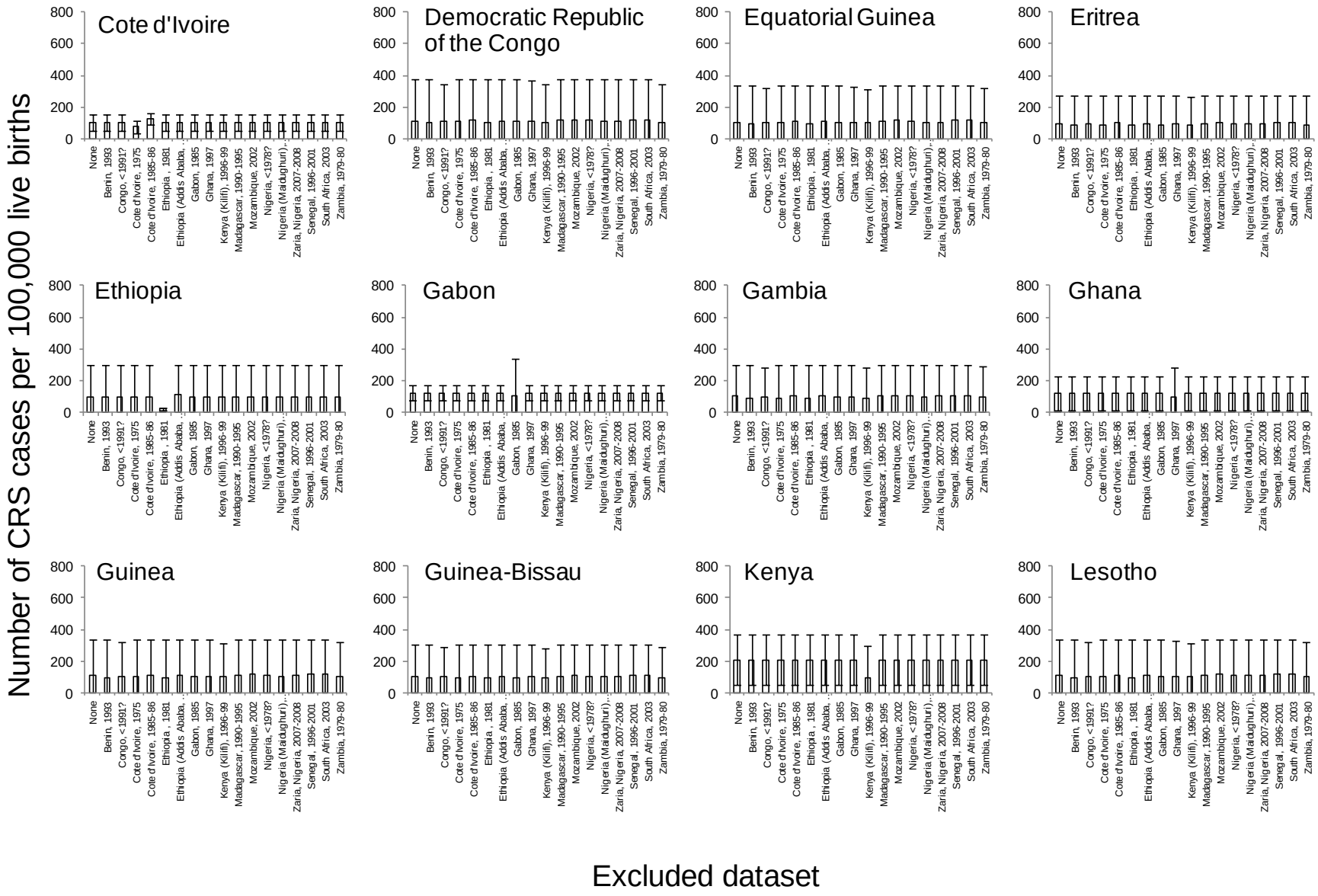

Figure G continued.

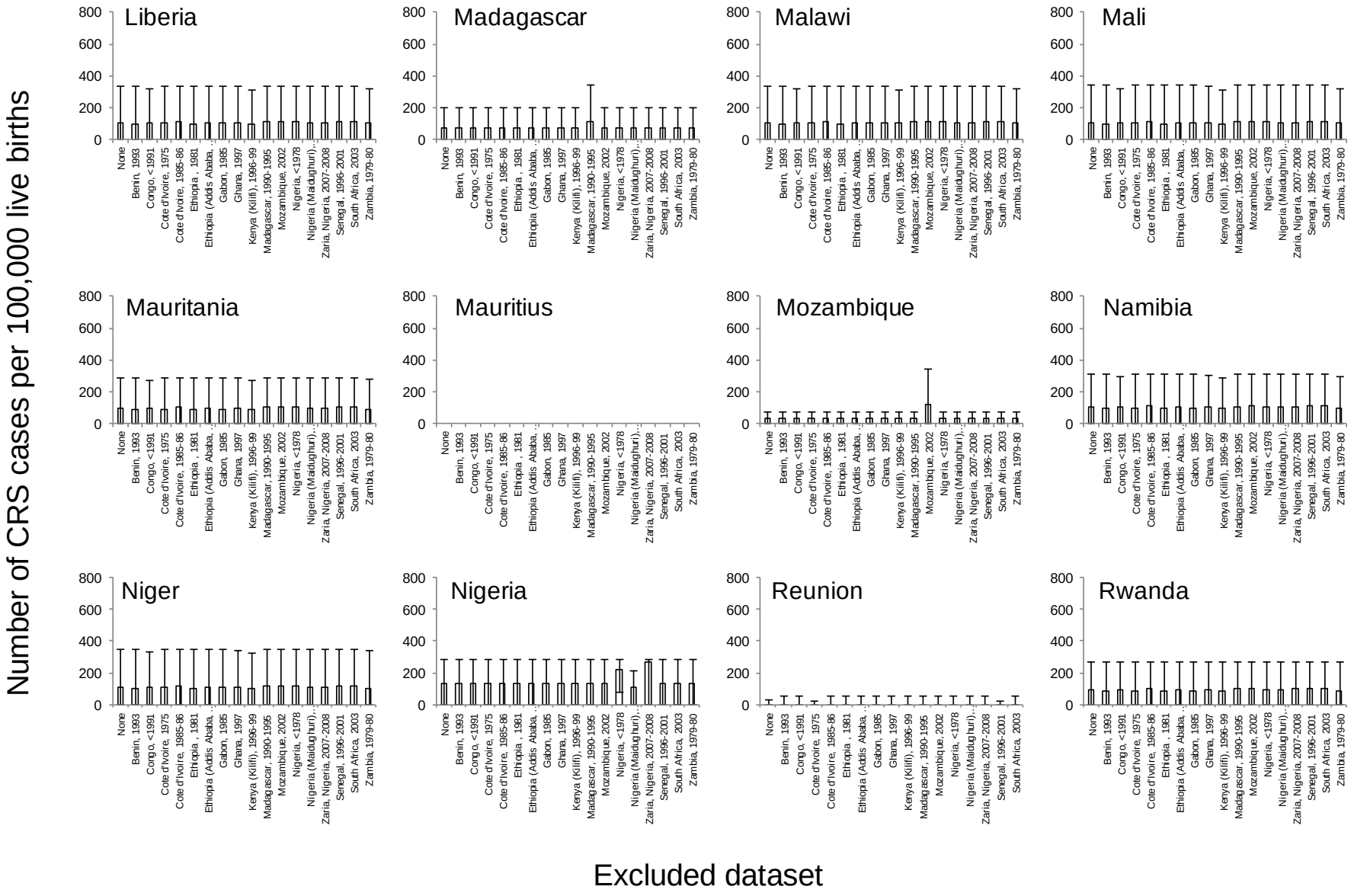

Figure G continued.

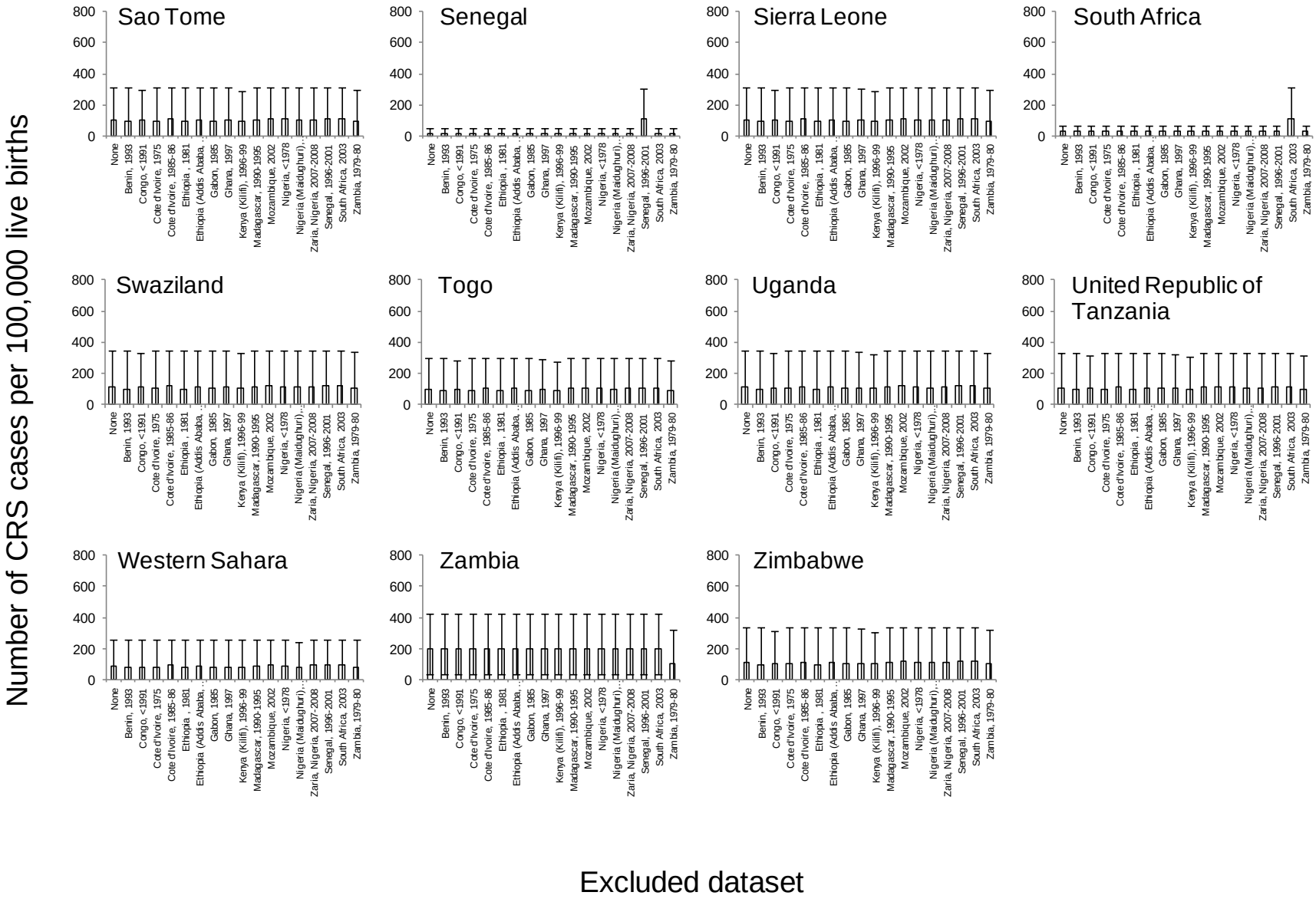

Figure G continued.

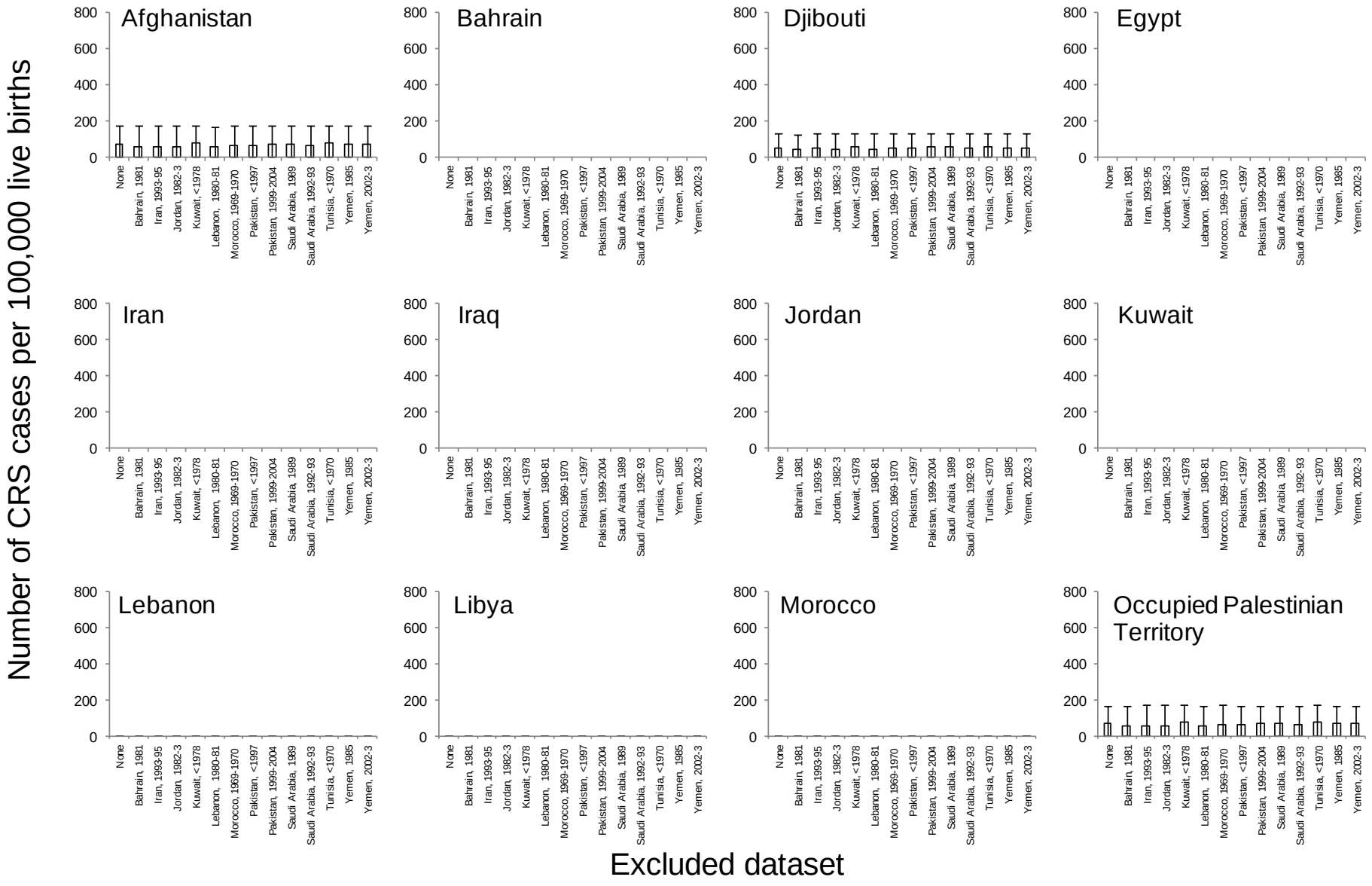

Figure H: Estimates of the country-specific CRS incidence per 100,000 live births in the Eastern Mediterranean in 2010, calculated after excluding individual datasets.

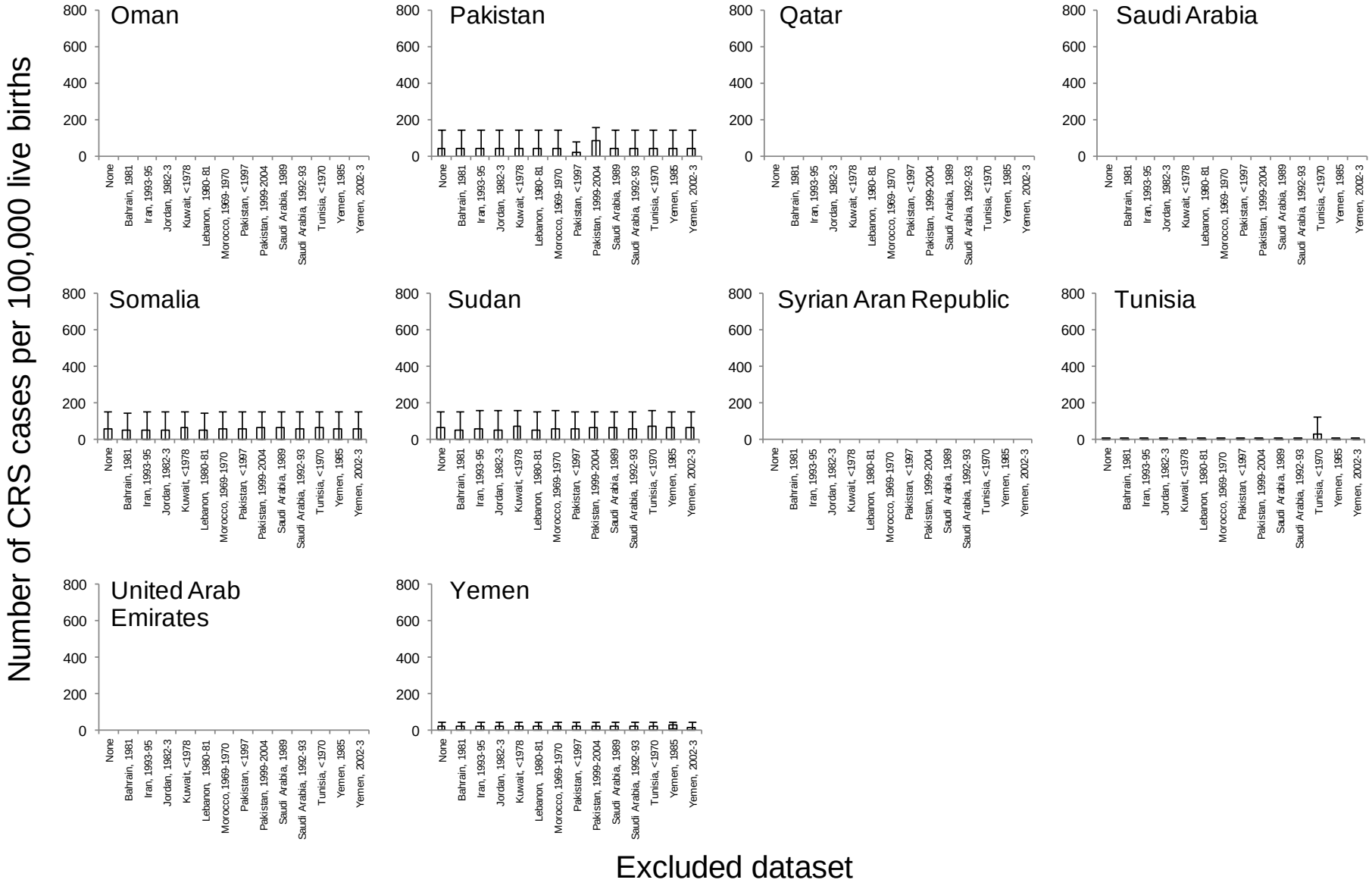

Figure H continued

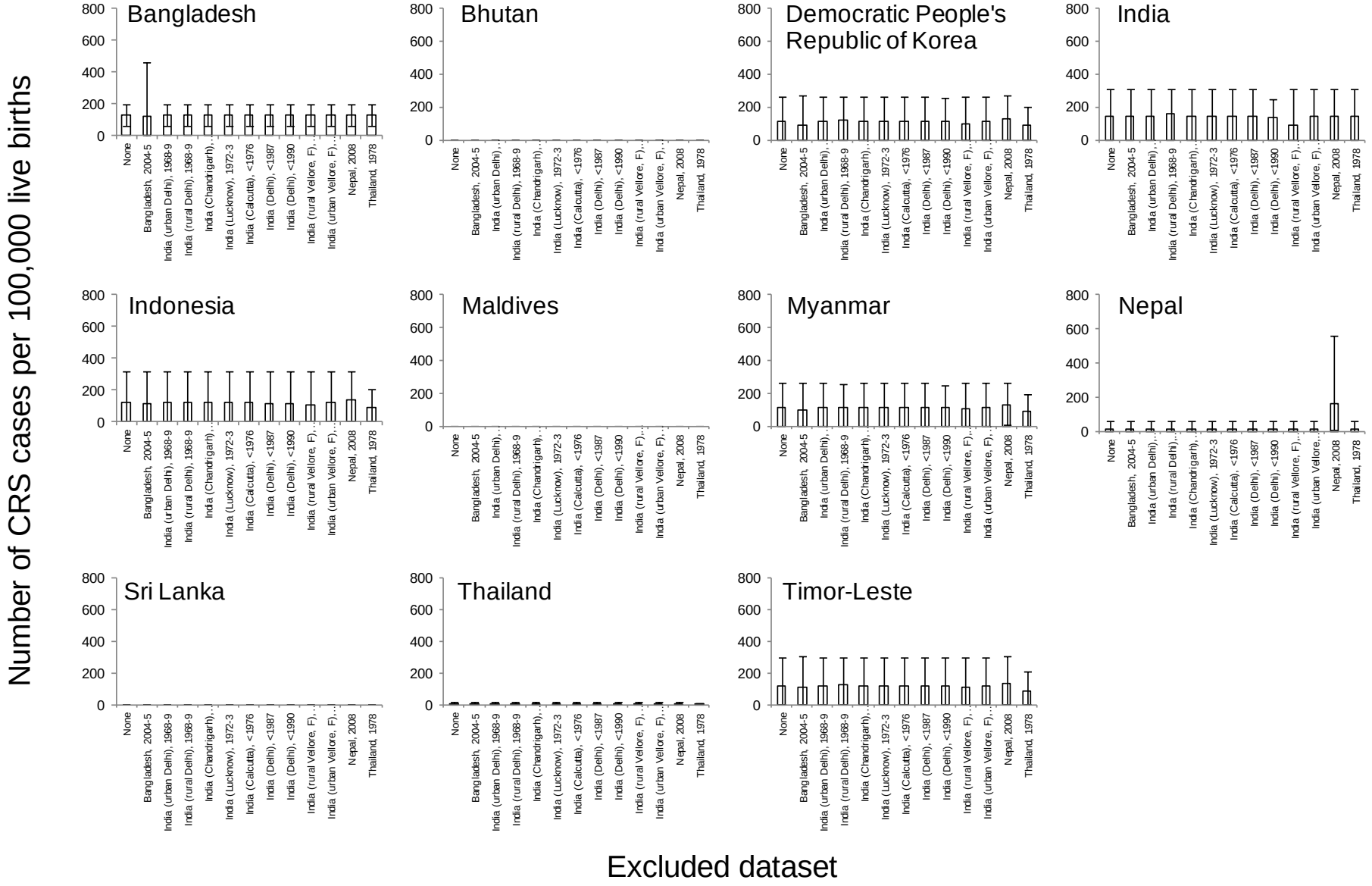

Figure I: Estimates of the country-specific CRS incidence per 100,000 live births in South East Asia in 2010, calculated after excluding individual datasets.

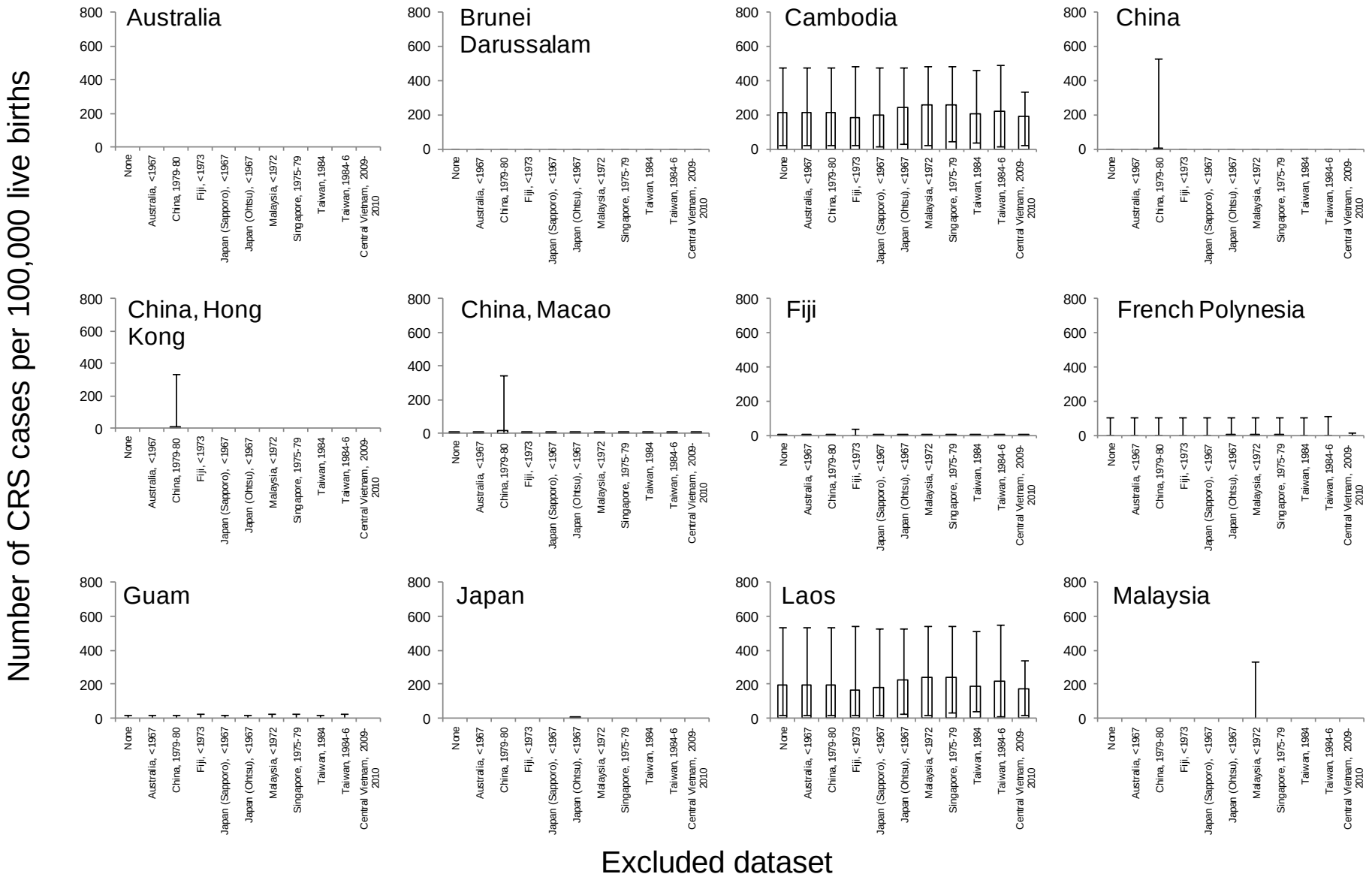

Figure J: Estimates of the country-specific CRS incidence per 100,000 live births in the Western Pacific in 2010, calculated after excluding individual datasets.

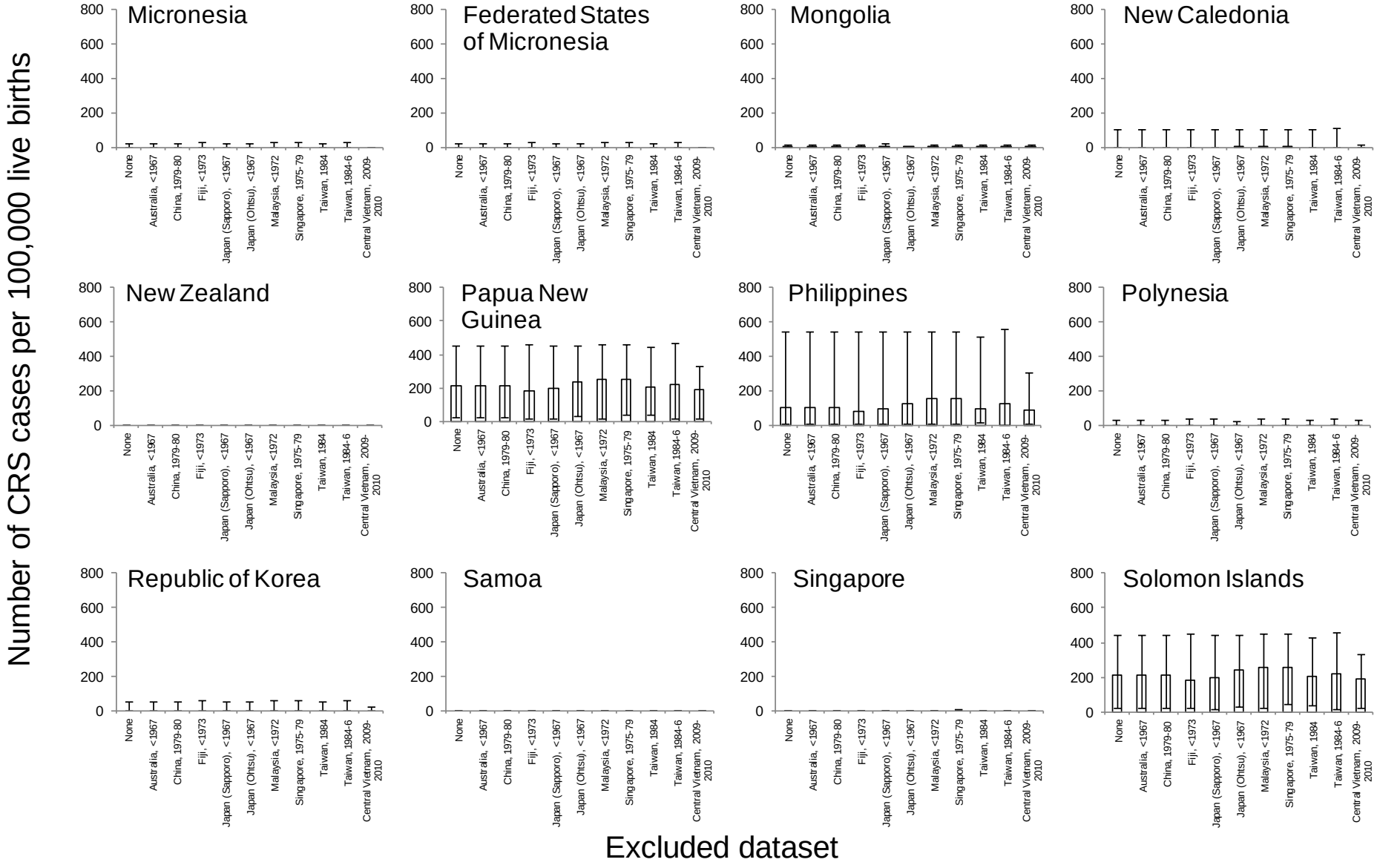

Figure J continued

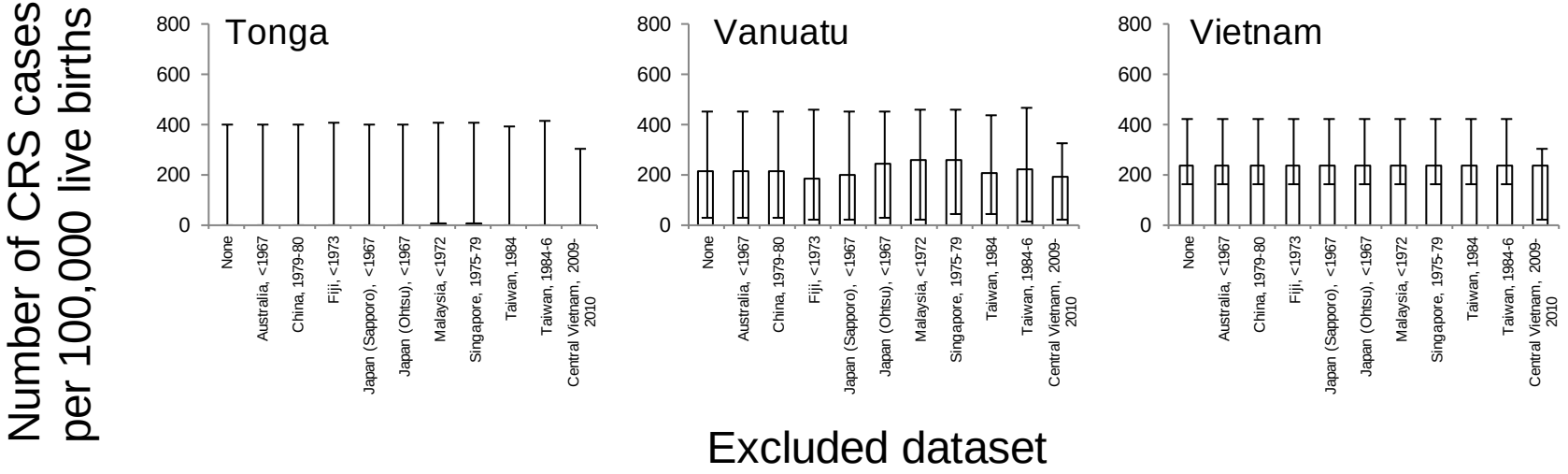

Figure J continued

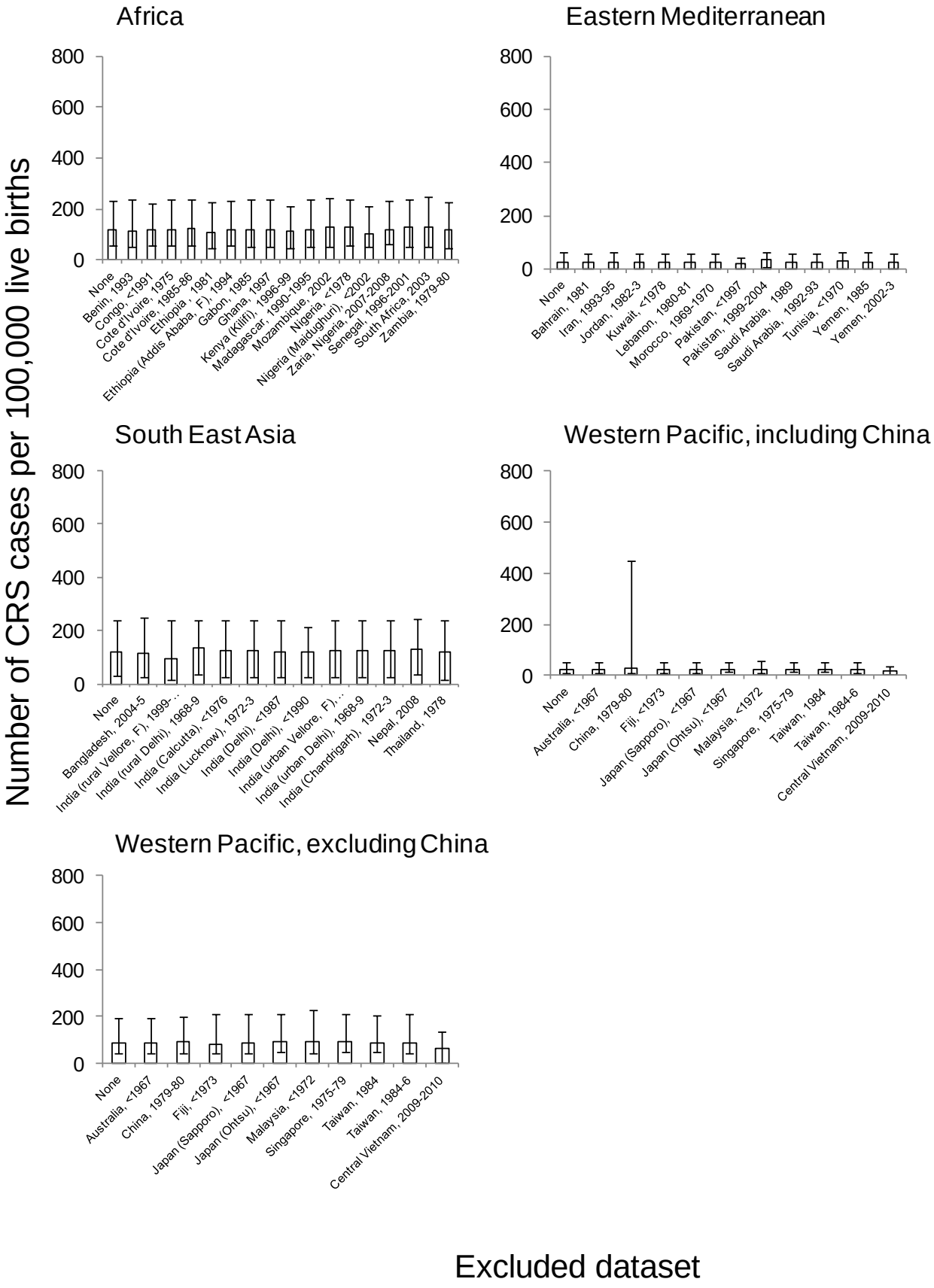

Figure K: Estimated CRS incidence per 100,000 live births among mothers aged 15-44 years in 2010 in the African, Eastern Mediterranean, South East Asian and Western Pacific regions, calculated after excluding individual datasets.

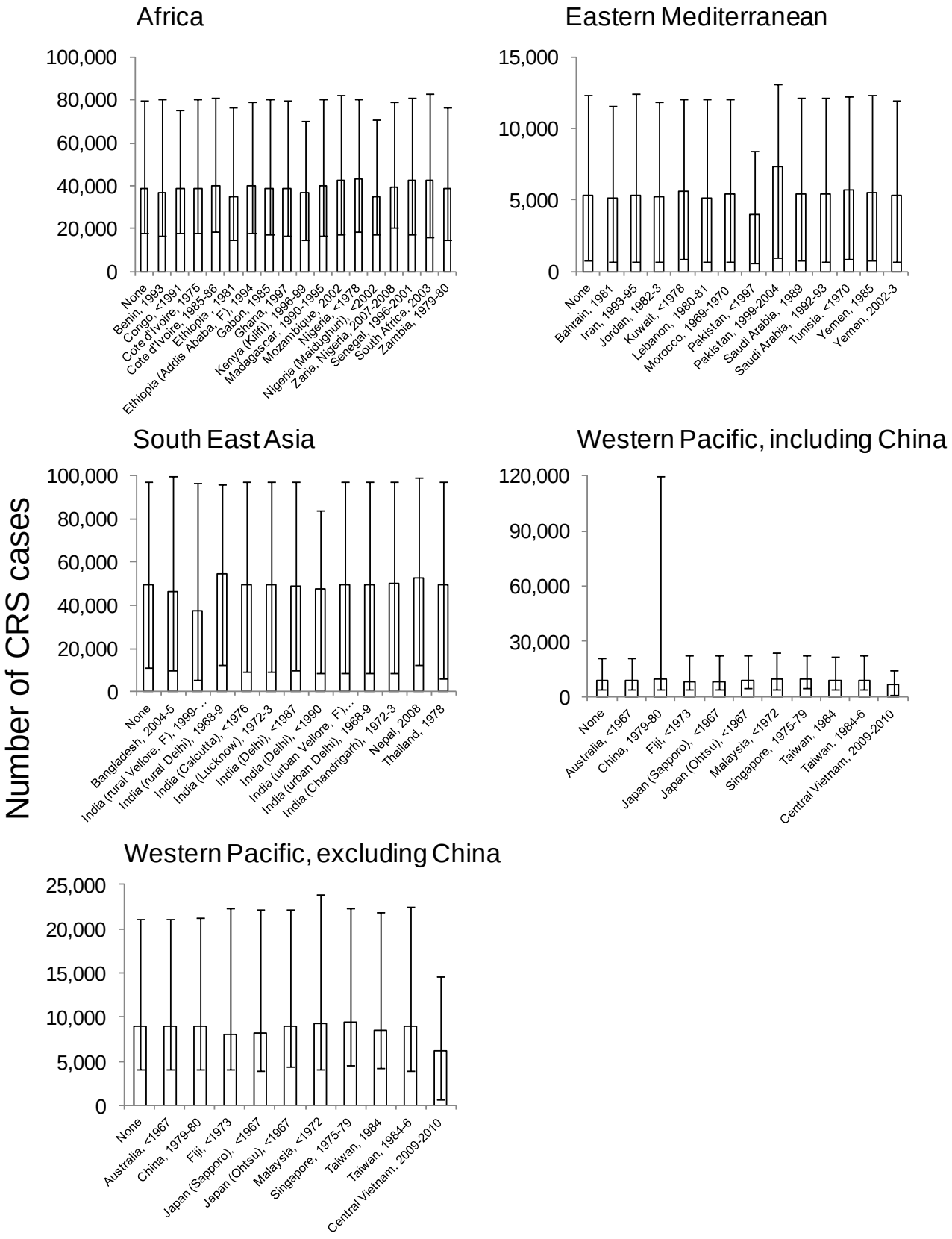

Figure L: Estimated numbers of CRS cases born among mothers aged 15-44 years in 2010 in the African, Eastern Mediterranean, South East Asian and Western Pacific regions, globally, calculated after excluding individual datasets.

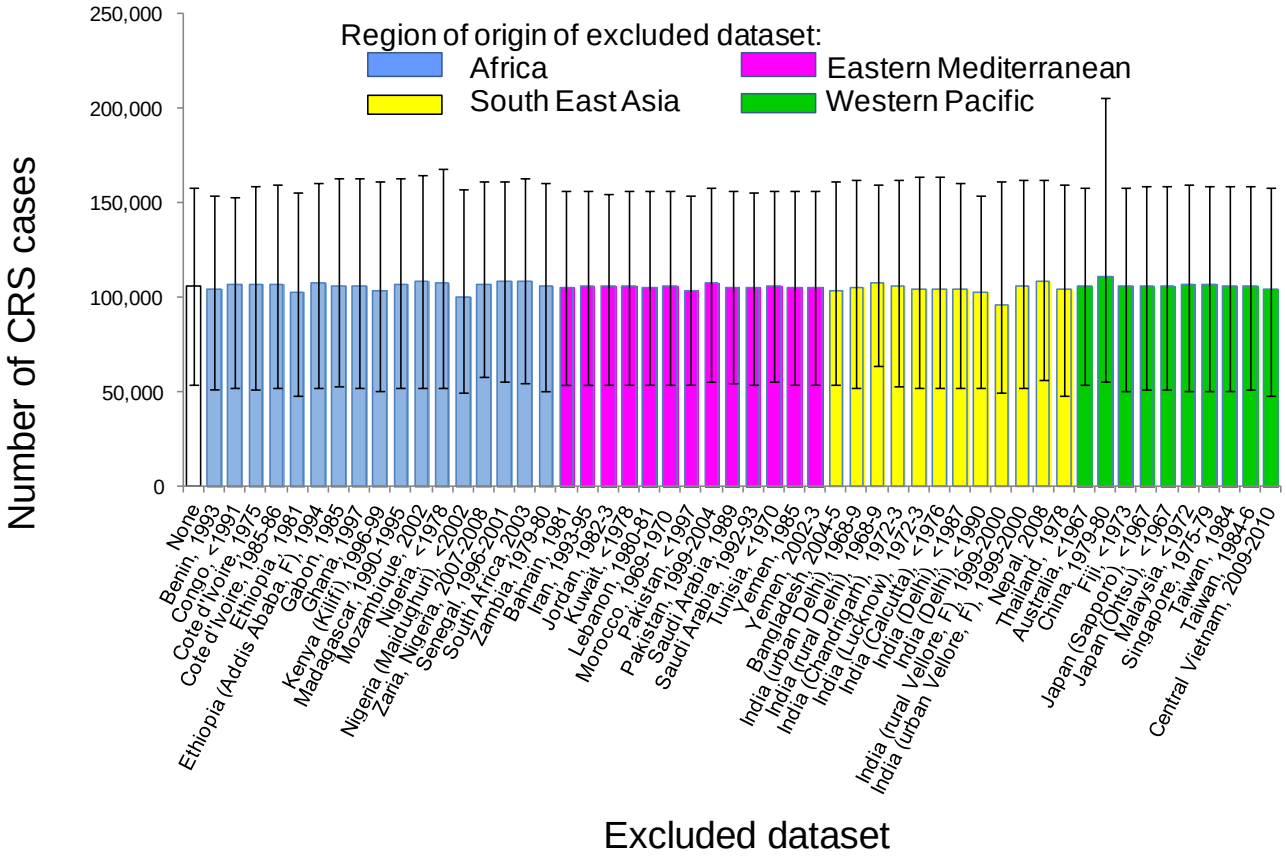

Figure M: Estimated numbers of cases of CRS born in 2010 globally, calculated after excluding individual datasets.

6.4 Comparison between the current and previous estimates obtained for 1996, for countries that had not introduced rubella-containing vaccine by 1996

In general, differences between the current and previous estimates for 1996, considering the countries analysed in previous analyses[99], varied between regions. The differences resulted mainly from the fact that previous estimates were based on comparatively fewer data sets and thus the incidence for many of the countries was assumed to equal the regional average. The latter was higher in previous analyses for some regions than in current settings, such as the Western Pacific. Other factors included the fact that the current estimates improved on those obtained previously by a) accounting for the sensitivity of the test (where possible), which led to increased or decreased estimates of the CRS burden for Mexico and China respectively, b) weighting the estimates by the age-dependent fertility rate, which led to increased estimates for some countries, e.g. the Philippines, c) accounting for the introduction of rubella-containing vaccine. Comparisons between the two sets of analyses are complicated by our use of the median, based on 1000 bootstrap-derived estimates, for the current analyses, whereas the previous analyses relied on average values. The differences for each region are described in further detail below and are summarised in Table M and Figure N.

For the African region, the previously predicted CRS incidence was slightly lower than that currently predicted: average of 104 vs median 116 per 100,000 live births respectively, corresponding to an average of 22,471 and median of 28,315 cases respectively. This discrepancy is largely due to the increased estimate for Nigeria in the current analyses (Figure N), which results mainly from the high incidence of CRS that was implied by one study[16], which had not been carried out at the time of the previous analyses. Likewise, differences between the estimates for the South East Asian region in 1996 were very small, with most of the small difference being attributable to increased numbers of cases in India, largely due to inclusion of additional datasets (Figure N).

For the American and Eastern Mediterranean regions, the CRS incidence was slightly lower that estimated previously (median of 10,553 vs an average of 15,995 for the American region and median

of 7,555 vs average of 12,080 for the Eastern Mediterranean). For the Americas, the estimates obtained for all countries (apart from Mexico) in the current analyses were smaller than those obtained previously. This partly resulted from the fact that, in contrast with previous analyses, the current analyses accounted for the sensitivity of the antibody assay, which resulted in force of infection estimates among older individuals being slightly higher than those obtained previously (e.g. 101 vs 28 per 1000 respectively using the data of Trujillo et al[26]). This increased force of infection, in turn, led to increased estimates of the CRS incidence.

For the Eastern Mediterranean region, the discrepancy was largely due to the estimate for Pakistan being reduced, as compared with that in previous analyses (Figure N), as a result of including datasets which have since become available[37-38]. Pakistan is one of the most populous countries in the Eastern Mediterranean, and this translated into a reduced estimate of the burden for this region.

For the Western Pacific Region, however, the estimates obtained using the two methods were similar (average total numbers of cases of 12,634 vs a median of 11,172, excluding China or 11,395, including China). As shown in Figure N the reduced estimates obtained for three countries (China, Korea and Malaysia) were compensated by increased estimates obtained for the Philippines. The increased estimates for the Philippines resulted from the fact that the numbers of CRS cases in the current analyses were calculated after weighting by an age-dependent fertility rate, which, in many regions, is highest in the youngest maternal age group, in which the incidence of CRS per 100,000 live births is also greatest. The reduced estimates for China resulted from including the sensitivity of the antibody assay when fitting the catalytic model to the data, which led to a slightly increased estimate of the prevalence of infection by child-bearing age. The reduced estimates for Malaysia and Korea resulted from including vaccination in these countries in the current modelling, whereas it was not included in previous analyses.

Table M: Comparison between estimates of the CRS incidence per 100,000 live births and the number of CRS cases born in 1996 in different regions. The values in the shaded rows are the values obtained in previous analyses by Cutts and Vynnycky[99]. The values in the rows labelled "restricted" refer to estimates obtained in the current analyses but considering only the countries used in previous analyses. The values in rows labelled "all" refer to estimates obtained in the current analyses and considering all countries.

Region	**Analysis**	**CRS incidence per 100,000 live births**			**Number of CRS cases**		
		Low*	"Average"+	High*	Low*	"Average"+	High*
AFRO	Cutts & Vynnycky (1999) [99]	25	104	246	6127	**22,471**	51,472
	restricted	55	115	231	13442	28308	57402
	all countries	55	115	231	13443	28315	57421
AMRO	Cutts & Vynnycky (1999)[99]: total Island: Mainland:	 0 0	 **171** **175**	 353 598	4552	**15,995**	35950
	restricted	36	89	167	4241	10553	19765
	all countries	24	56	104	4394	10640	19867
EMRO	Cutts & Vynnycky (1999) [99]	0	**77**	212	1008	**12080**	30711
	restricted	22	56	106	2568	7555	15135
	all countries	22	56	106	2577	7625	15290
SEARO	Cutts & Vynnycky (1999) [99]	0	**136**	470	1016	**46,621**	168,910
	restricted	43	130	251	14553	50076	96372
	all countries	43	130	251	14587	50128	96435
WPRO	Cutts & Vynnycky (1999) [99]	0	**173**	302	1545	**12,634**	21396
	restricted	91	188	351	5193	11395	21179
	all countries	58	118	225	5268	11541	21980
Global	Cutts & Vynnycky (1999) [99]				14248	**109,800**	308,438
	restricted				64303	111428	161552
	all countries				72119	119224	169107

* Low and high refer to the minimum and maximum values presented in the previous analyses[99] and to the lower and upper limits of the 95% CI, based on bootstrapping, for the current analyses.

+ The average refers to the "mean" value in the previous analyses[99] and to the median, based on 1000 bootstraps in the current analyses.

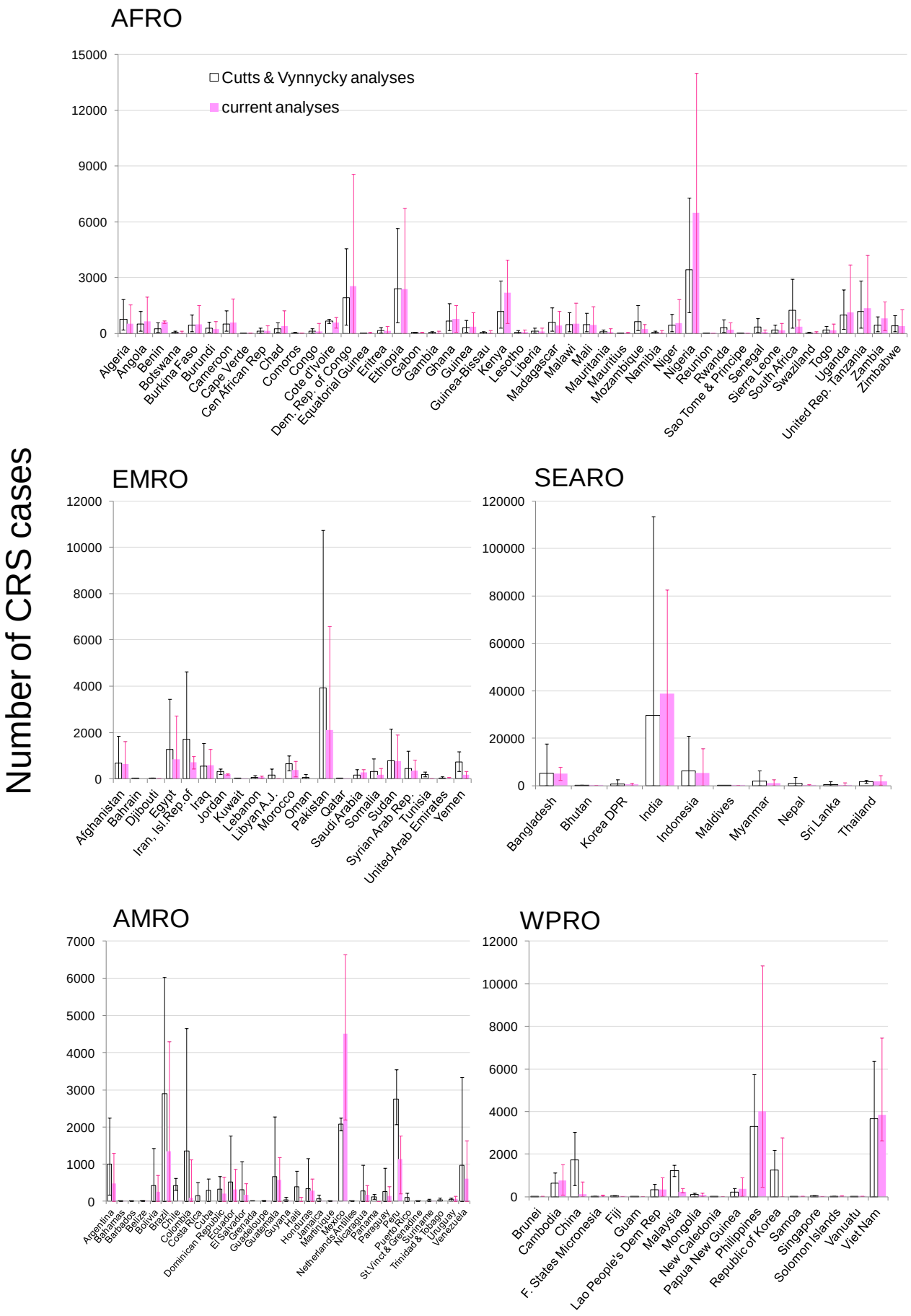

Figure N: Comparison between the numbers of CRS cases estimated in the current analyses for 1996 against those obtained for 1996 by Cutts and Vynnycky[34].

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