Report for the SAGE Working Group on Measles and Rubella

The Roadmap to Immunity

Appendix 1. Examples of Data Sources and Methods to Estimate Immunity Gaps

Case-Based Surveillance Data

Example 1: This paper analyzed case-based surveillance data from 1989-2001 to calculate measles incidence by age group in Turkey (based upon clinical findings; lab confirmation was rare). Since 1989, the majority of measles cases have been among children <15 years old. During most years, 90%-95% of all measles cases were <15 years of age. In 1997, an epidemic year, 85% of cases were <15 years old. Cases aged 1-4 years and 5-14 years comprised 20%–36% and 43%–65%, respectively, of all cases reported each year. Overall, the highest incidence was in children aged <1 year and 5-9 years; lowest incidence was among adolescents and adults ≥15 years old.

Turkey's Ministry of Health launched a comprehensive program for 2002-2010 targeting measles elimination, and called for a high-coverage (≥95%) national mass vaccination campaign among all children aged 9 months to 14 years. The paper additionally recommended achieving ≥95% two-dose coverage, vaccination of all military recruits, ongoing monitoring of accumulation of susceptible children, and periodic supplemental vaccinations as needed.

Reference: Guris D, et al. Measles epidemiology and elimination strategies in Turkey. J Infect Dis. 2003 May;187 Suppl 1:S230-234.

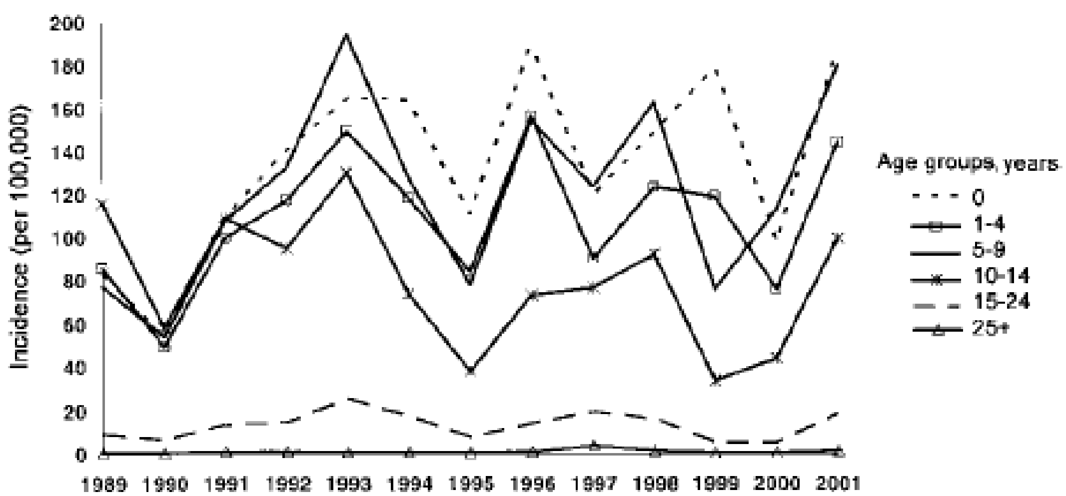


Figure 4. Measles incidence by age group, Turkey, 1989–2001

Example 2: This paper analyzed case-based surveillance data from Mazandaran province, Iran, during 2000-2002. It found that 42.7% of the total cases occurred in 10-19-year-olds (who should have received two doses of vaccine), and 21.2% were in adults older than 20 years (who should have received one dose of vaccine after 12 months of age). Because of the observed high incidence of measles in those who should have been vaccinated, the paper recommends catch-up immunization and revaccination of young adults to boost immunity. Primary and secondary vaccine failures were noted as a concern, and the paper also recommends attention on proper shipping and storing of vaccine.

In 2002 Iran's Ministry of Health and Medical Education (MOHME) developed a plan for measles elimination that included conducting a nationwide measles immunization campaign in 2003 using a combined measles and rubella vaccine for all persons aged 5–25 years, a target population representing about 50% of the total population of Iran.

References:

1) Saffar MJ, et al. Measles epidemiology in Mazandaran province, Iran, 2000-2002. Trop Doct. 2007 Jan;37(1):30-32.
2) Zahraei SM, et al. Successful control and impending elimination of measles in the Islamic Republic of Iran. J Infect Dis. 2011 Jul;204 Suppl 1:S305-11.

Table 1 Relationship between disease occurrence and age during the 3 years of the study, Mazandaran 2000–2002

	Years			
	2000 (%)	*2001 (%)*	*2002 (%)*	*Total (%)*
Age group	*n=162*	*n=269*	*n=298*	*n=729*
Less than 12 months	6 (3.7)	35 (13)	26 (8.7)	67 (9.2)
1–4 years	7 (4.3)	29 (10.8)	26 (8.7)	62 (8.5)
5–9 years	11 (6.8)	69 (25.6)	54 (18.1)	134 (18.4)
10–19 years	76 (46.9)	100 (37.1)	135 (45.3)	311 (42.7)
20 years and older	62 (38.2)	36 (13.4)	57 (19.1)	155 (21.2)
Total	162 (100)	269 (100)	298 (100)	729 (100)

Example 3: This paper analyzed the epidemiology of rubella surveillance data in Singapore during 1991-2007. Rubella incidence was highest in preschool children aged <5 years (24.1% - 38.1% of reported cases), except in 1999 and 2000 when there were higher proportions of adolescent and adults cases due to institution-based outbreaks (foreign students, office and factory workers). Most of the cases among children <5 years were infants <1 year of age (55%) who were below the age of vaccination.

Reference: Ang LW, et al. Epidemiological surveillance and control of rubella in Singapore, 1991-2007. Ann Acad Med Singapore. 2010 Feb;39(2):95-101.

Table 1. Age-Specific Incidence Rates per 100,000 Population of Reported Rubella Cases, 1998-2007

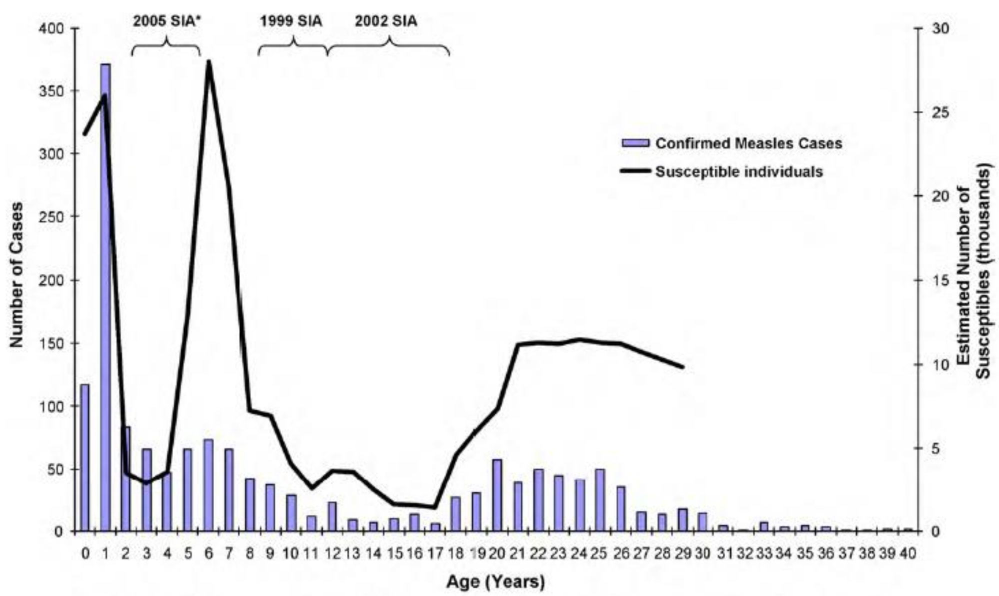
Age group (y)	1998 (n = 179)	1999 (n = 432)	2000 (n = 312)	2001 (n = 242)	2002 (n = 152)	2003 (n = 88)	2004 (n = 141)	2005 (n = 139)	2006 (n = 90)	2007 (n = 83)
0-4	21.5 (30.2)	11.5 (6.5)	2.5 (1.9)	28.0 (27.3)	25.2 (38.1)	14.5 (36.4)	15.7 (24.1)	19.4 (29.5)	14.9 (34.4)	11.0 (27.7)
5-9	4.4 (6.7)	3.3 (2.1)	6.7 (5.8)	5.6 (6.2)	4.1 (7.2)	1.2 (3.4)	0.4 (0.7)	2.8 (5.0)	1.2 (3.4)	0.0 (0.0)
10-14	6.6 (8.4)	7.8 (4.4)	25.3 (20.2)	6.1 (6.6)	10.7 (19.1)	2.9 (9.1)	3.7 (7.1)	2.6 (5.0)	1.5 (4.4)	1.1 (3.6)
15-24	5.2 (17.9)	20.5 (28.7)	13.2 (26.3)	6.4 (16.9)	4.2 (17.1)	2.3 (15.9)	3.7 (16.3)	2.9 (13.7)	2.8 (21.1)	2.5 (21.7)
25-34	3.9 (19.5)	11.3 (22.9)	11.3 (31.7)	5.2 (19.0)	1.9 (11.2)	2.0 (19.3)	4.0 (24.1)	3.4 (20.9)	2.5 (24.4)	2.2 (25.3)
35-44	2.9 (11.7)	12.2 (21.1)	4.6 (11.2)	5.8 (18.6)	1.3 (6.6)	1.1 (9.1)	2.5 (13.5)	2.9 (15.8)	0.4 (3.4)	0.9 (8.4)
45-54	1.1 (5.6)	6.3 (14.3)	0.9 (2.9)	1.2 (5.4)	0.1 (0.7)	0.5 (6.8)	1.7 (14.2)	1.1 (10.1)	0.6 (8.9)	0.8 (13.3)
Total	4.6 (100.0)	10.9 (100.0)	7.7 (100.0)	5.8 (100.0)	3.6 (100.0)	2.1 (100.0)	3.4 (100.0)	3.3 (100.0)	2.0 (100.0)	1.8 (100.0)

Figures in brackets refer to percentage of total cases in the corresponding year.

Outbreak Investigations

Example 4: This investigation of an outbreak in Dar es Salaam, Tanzania during 2006-2007 shows the distribution of confirmed measles cases by age in years. Cases peaked among those <2 years, 5-7 years, and 18-30 years. Case peaks matched well to a modeled susceptibility distribution that was based on the combined non-vaccination of individuals through routine services and SIAs. In response to the outbreak and based in part on results from the outbreak investigation, a sub-national campaign was conducted in 2006 in Dar es Salaam targeting children 6 months to 14 years, and a nationwide follow-up immunization campaign was conducted in 2008 targeting children 6 months to 10 years of age. This example shows that it is possible to control measles by immunizing younger age groups even when there are gaps in older age groups.

Reference: Goodson JL, et al. Measles outbreak in Tanzania, 2006-2007. Vaccine. 2010 Aug;28(37):5979-5985.



*Supplemental immunization activity; the bracket indicates the age group targeted by the SIA.

Fig. 3. Confirmed measles cases ($N = 1533$) and estimated susceptible individuals ($N = 272,435$) by age, Dar es Salaam, Tanzania, July 2006–January 2007. *Supplemental immunization activity; the bracket indicates the age group targeted by the SIA.

Example 5: This descriptive epidemiological analysis of a measles outbreak in Namibia during 2009-2011 used case-based surveillance and laboratory data. Infants ≤11 months were heavily affected by the outbreak (22% of all cases, highest cumulative age-specific incidence), but cases were widely distributed across all ages, indicating that measles-susceptible individuals accumulated over several decades prior to the start of the outbreak.

In response to the outbreak, an outbreak response immunization campaign was conducted in the six districts most affected by the outbreak in September-December 2009; it targeted children aged 6-59 months who had never been vaccinated. In February 2010 additional ORI activities were conducted in a high-incidence district targeting everyone aged 6 months or older irrespective of previous vaccination status, and during March 2010, ORI campaigns were conducted in 3 more districts, targeting individuals aged 6 months to 35 years.

Reference: Ogbuanu IU, et al. Measles outbreak reveals measles susceptibility among adults in Namibia, 2009 - 2011. S Afr Med J. 2016 Jun;106(7):715-720.

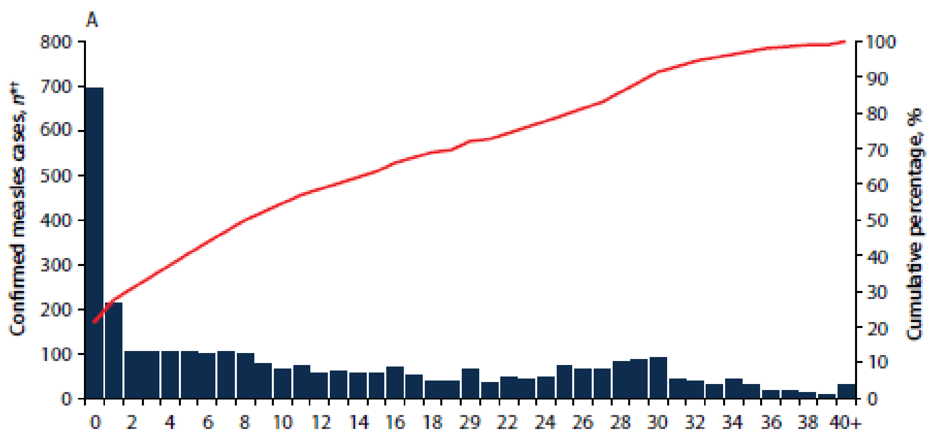


Fig. 3. Confirmed measles cases (N=3 233[†]) by age in years, Namibia, 2 August 2009 - 2 February 2011: A = Namibia; B = Windhoek; and C = Opuwo. (*Confirmed measles cases were defined by laboratory confirmation or epidemiological link. [†]23 confirmed cases had missing age information.)*

Example 6: An investigation of a measles outbreak in Mongolia during 2001 found two peaks in age-specific incidence, one in infants <1 year of age and another in young adults 15-24 years of age. The age distribution of this outbreak could have been a result of the country's vaccination programs; children aged 2-14 years were likely protected because they had been vaccinated 3-4 times during 1994-2000, while young adults aged 15-24 years were vaccinated only once as infants, and vaccination coverage during the 1980s was not well documented. The paper concludes that "immunization strategies such as the age range that is targeted for vaccination and the interval between supplemental immunizations should be based on reasonable epidemiological observations."

Reference: Rentsen T, et al. Measles outbreak after a post-honeymoon period in Mongolia, 2001. Jpn J Infect Dis. 2007 Jul;60(4):198-199.

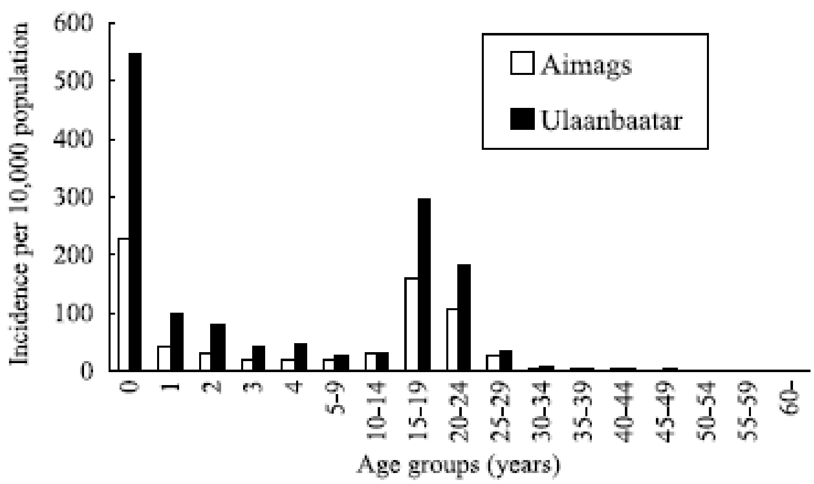


Fig. 2. Measles incidence by age groups in Aimags and Ulaanbaatar in Mongolia, 2001. Incidence was calculated from the number of reported measles cases during 2001.

Example 7: This investigation of a rubella outbreak in Kyrgyzstan in 2001 found that most cases were 3-14 years old, but the incidence rate among persons aged 15-35 years increased ≥40-fold from 2000 to 2001. A “catch-up” measles vaccination campaign had previously been planned for November 2001 targeting children and young adults aged 7-25 years. After this rubella outbreak, combined MR vaccine was used in the catch-up vaccination campaign in November 2001, and since January 2002 MMR vaccine has been in the national vaccination program in a two-dose schedule (i.e., administered at ages 1 and 6 years).

Reference: Dayan GH, et al. Investigation of a rubella outbreak in Kyrgyzstan in 2001: implications for an integrated approach to measles elimination and prevention of congenital rubella syndrome. J Infect Dis. 2003 May;187 Suppl 1:S235-240.

Table 1. Age distribution of reported rubella cases, Bishkek City, Chui Oblast, Kyrgyzstan, January–August 2001.

	Bishkek City		Chui Oblast		Total	
Age group (years)	No. of case-patients (%)[a]	IR/100,000	No. of case-patients (%)[a]	IR/100,000	No. of case-patients (%)	IR/100,000
Unknown	11 (1)		2 (0.5)		13 (1)	
0–2	89 (6)	309	12 (3)	35	101 (5)	161
3–6	562 (38)	1363	90 (20)	178	652 (34)	710
7–14	660 (44)	710	275 (61)	222	935 (48)	431
15–25	147 (10)	81	67 (15)	50	214 (11)	68
26–49	19 (1)	5	2 (0.5)	0.5	21 (1)	3
Total	1488 (100)	196	448 (100)	61	1936 (100)	129

NOTE. IR, incidence rate.

[a] χ^2 test of homogeneity, 10.33; $P < .05$.

Example 8: During an import-related measles epidemic in Quebec, Canada in 2011, the highest incidence was among adolescents aged 12-17 years (comprising 56% of all cases). The investigation found susceptibility to measles among adolescents who had received two doses of vaccine. Among adolescent cases, 22% had received 2 vaccine doses, and through active case finding, this proportion was found to be an underestimate; 130% more cases were identified among 2-dose recipients (tended to have had milder illness and a lower risk of hospitalization). Immunization coverage was very high in this outbreak; a high proportion of fully vaccinated cases is expected when coverage is high. This epidemic was considered a “superspreading event” and occurred in the context of accumulated susceptibility in students who themselves had ample transmission possibilities through their rich social networks.

Reference: De Serres G, et al. Largest measles epidemic in North America in a decade--Quebec, Canada, 2011: contribution of susceptibility, serendipity, and superspreading events. J Infect Dis. 2013 Mar;207(6):990-998.

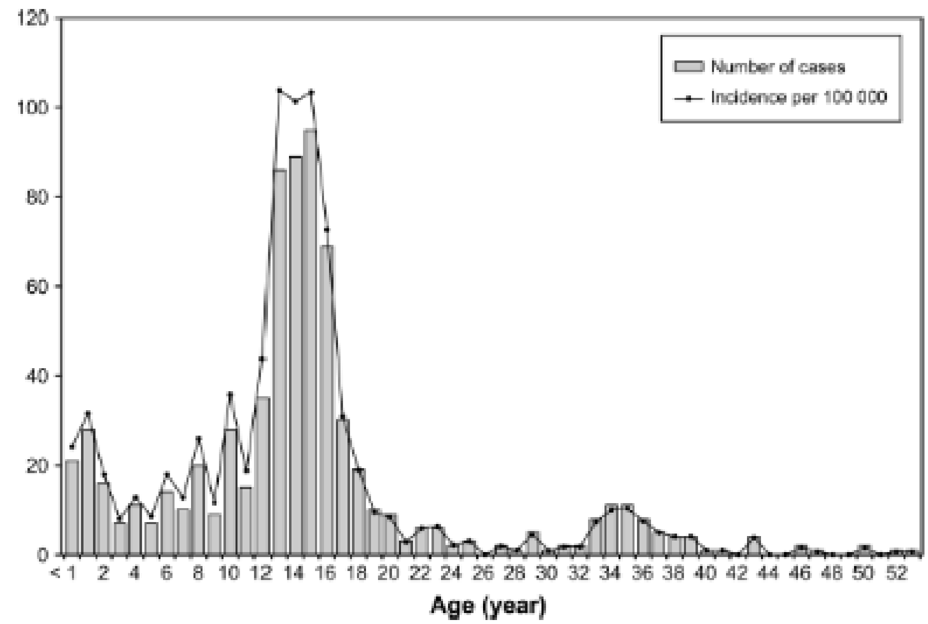
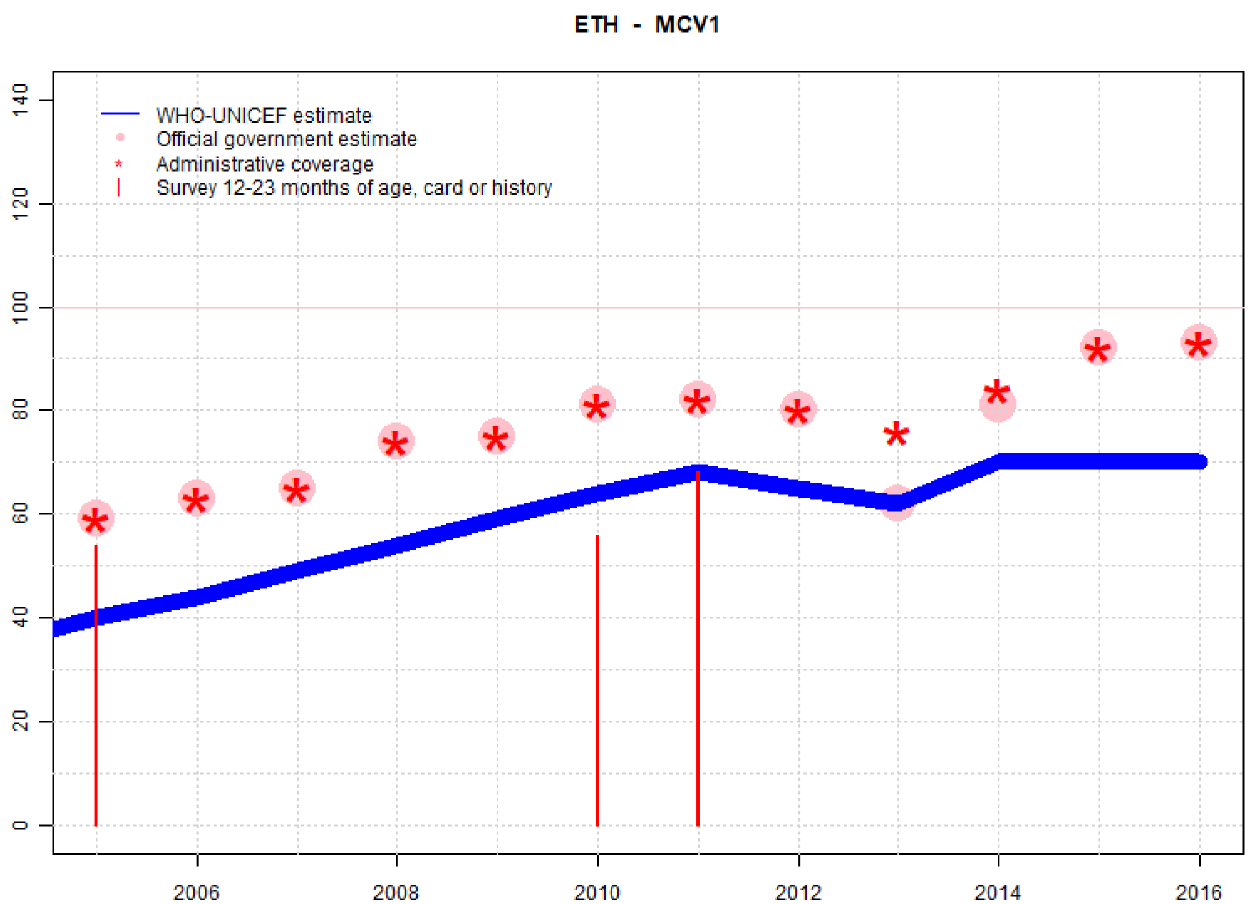


Figure 2. Number and incidence of measles cases by patient age.

Historical Coverage Data (Administrative and WUENIC)

Example 9: The WHO publishes annual reported coverage data and WUENIC estimates on their website each year. Looking at Ethiopia's MCV1 coverage from 2005-2016, administrative coverage has risen from ~60% to ~93% while WUENIC estimates have only reached ~70%. While the administrative coverage suggests they are approaching the target of 95%, the WUENIC estimates suggest that a large proportion of each birth cohort is still not receiving MCV1 vaccine and that high quality follow-up campaigns are needed along with strengthening of routine immunization.

Reference: WHO and UNICEF estimates of immunization coverage available at:
http://www.who.int/immunization/monitoring_surveillance/data/eth.pdf



<u>Population Coverage Surveys (Including Post-Campaign, Multiple Indicator Cluster Surveys (MICS, Demographic Health Surveys (DHS) etc.)</u>

Example 10: The table below is from the 2013-14 Demographic and Health Survey (DHS) in the Democratic Republic of Congo (DRC). It shows the number of caregivers of 12-23 month old children reporting that their child had received the specified vaccine at some point prior to the survey (according to the vaccination card or parental recall), stratified by sex, birth order, province, mother's education level, and socio-economic quintile.

Note: The official and WUENIC estimates for MCV1 in DRC in 2014 were 89% and 77%, respectively. The DHS estimate for MCV1 for children aged 12-23 months was 71.6%.

Reference: Demographic and Health Survey (DRC-DHS II) 2013-2014, available at: https://www.dhsprogram.com/pubs/pdf/FR300/FR300.pdf

Tableau 10.3 Vaccinations selon certaines caractéristiques sociodémographiques

Pourcentage d'enfants de 12-23 mois ayant reçu certains vaccins à n'importe quel moment avant l'enquête (selon le carnet de vaccination ou la déclaration de la mère) et pourcentage pour lesquels un carnet de vaccination a été présenté à l'enquêtrice, selon certaines caractéristiques sociodémographiques, République Démocratique du Congo 2013-2014

Caractéristique sociodémographique	BCG	DTC/Pentavalent[1]			Polio				Rougeole	Tous les vaccins[3]	Aucun vaccin	Fièvre Jaune	Pourcentage avec un carnet de vaccination présenté à l'enquêtrice	Effectif d'enfants
		1	2	3	0[2]	1	2	3						
Sexe														
Masculin	83,5	81,2	73,6	60,0	48,6	92,3	84,2	64,2	72,1	45,1	5,7	65,7	25,9	1 687
Féminin	83,3	81,3	74,1	61,1	51,1	91,1	84,7	67,1	71,1	45,5	6,1	65,2	26,2	1 680
Rang de naissance														
1	85,9	84,3	76,7	63,0	52,3	93,0	83,8	66,8	75,2	49,2	4,0	67,1	31,7	657
2-3	83,9	80,6	73,3	59,5	48,6	90,6	84,0	65,7	72,2	43,5	6,3	66,5	23,9	1 088
4-5	82,9	81,9	75,2	61,7	51,1	91,2	84,2	62,6	71,7	45,4	6,4	68,4	24,5	790
6+	81,4	79,0	70,9	59,0	48,5	92,4	85,8	67,6	68,0	44,3	6,4	59,9	25,9	832
Résidence														
Urbain	92,1	92,1	86,1	74,2	69,1	94,4	88,8	71,7	77,3	53,0	2,8	72,9	34,9	1 083
Rural	79,3	76,1	68,0	54,1	40,7	90,3	82,4	62,8	68,9	41,6	7,3	61,9	21,8	2 284
Province														
Kinshasa	96,7	97,8	95,8	83,7	82,5	97,1	93,3	80,2	89,0	67,7	0,9	86,7	43,9	267
Bas-Congo	95,6	93,5	90,2	84,1	69,5	96,1	92,0	61,0	84,6	54,7	2,5	85,5	32,2	161
Bandundu	89,8	87,5	80,1	61,9	42,2	92,9	86,5	57,7	77,3	42,1	3,9	72,9	16,4	559
Équateur	72,1	68,7	56,9	42,6	31,7	89,6	82,8	64,5	66,1	32,6	7,6	53,2	22,7	493
Orientale	74,5	70,5	60,0	46,0	39,2	84,8	74,7	52,9	67,4	29,9	11,8	53,1	12,7	315
Nord-Kivu	95,1	94,4	91,1	87,0	73,9	94,8	89,0	75,0	85,3	70,6	3,1	85,2	44,2	288
Sud-Kivu	95,6	95,1	88,5	75,6	62,1	94,5	86,9	75,5	87,8	62,3	2,9	84,2	42,4	231
Maniema	72,2	73,8	66,7	47,2	37,5	89,2	81,0	64,5	62,3	42,0	10,7	55,3	17,7	115
Katanga	69,2	67,3	60,1	51,3	43,0	91,0	83,9	70,9	53,0	40,2	7,7	44,6	23,4	358
Kasaï Oriental	81,3	76,7	69,3	53,3	45,5	89,0	78,8	62,0	58,2	36,6	8,8	54,6	18,7	361
Kasaï Occidental	84,8	82,2	72,7	56,2	51,9	92,8	84,3	67,7	67,3	42,7	3,7	62,4	30,9	218
Niveau d'instruction de la mère														
Aucun	77,4	74,3	68,2	56,8	43,3	89,7	82,4	63,2	65,4	42,4	8,1	59,1	20,9	605
Primaire	79,0	75,6	65,6	52,0	42,8	90,6	81,4	61,5	65,5	37,6	7,7	58,8	20,1	1 431
Secondaire	90,6	90,1	84,7	70,4	59,5	93,5	88,5	70,9	80,1	53,7	3,1	74,4	33,7	1 271
Supérieur	(99,4)	(99,4)	(96,3)	(93,1)	(80,3)	(97,2)	(93,7)	(78,9)	(99,4)	(77,9)	(0,6)	(99,4)	(56,9)	60
Quintiles de bien-être économique														
Le plus bas	74,1	69,3	61,0	48,0	34,1	88,4	81,2	60,0	61,8	36,1	9,7	54,7	16,3	748
Second	80,6	76,0	65,8	50,7	41,2	90,0	80,3	58,2	67,3	36,4	6,9	58,8	19,6	741
Moyen	81,3	79,5	72,9	56,5	46,3	89,7	82,6	64,4	72,6	43,7	6,6	65,9	27,7	645
Quatrième	88,1	88,7	81,9	69,8	56,8	95,2	87,7	68,6	75,2	49,5	3,4	70,4	28,2	636
Le plus élevé	96,0	96,7	92,4	83,0	76,8	96,2	92,2	80,3	84,3	65,0	1,7	81,3	42,2	596
Ensemble	83,4	81,2	73,8	60,5	49,9	91,7	84,5	65,6	71,6	45,3	5,9	65,4	26,0	3 366

Note : Les valeurs entre parenthèses sont basées sur 25-49 cas non pondérés.
[1] Le Pentavalent comprend la diphtérie, le tétanos, la coqueluche, *l'Haemophilus influenzae type B* (Hib) et l'hépatite B.
[2] Polio 0 est le vaccin contre la polio donné à la naissance.
[2] BCG, rougeole, les trois doses de Pentavalent et les trois doses de polio (non compris la dose de polio donnée à la naissance).

Serosurveys

Example 11: Serosurvey conducted as part of 2013-14 DHS in the Democratic Republic of Congo (DRC) showing the prevalence of measles IgG antibodies in serum collected from children at 6-59 months, stratified by sex, age group, urban/rural residence, and province of residence.

Note: The official and WUENIC estimates for MCV1 in DRC in 2014 were 89% and 77%, respectively. The DHS estimate for MCV1 for children aged 12-23 months was 71.6%.

Reference: Demographic and Health Survey (DRC-DHS II) 2013-2014, Supplemental Vaccine-preventable Diseases Report available at: https://www.dhsprogram.com/pubs/pdf/FR300/FR300.vpd.pdf

Table 2 Results estimating the presence of measles antibodies

Distribution of children 6-59 months tested for the presence of measles antibodies, by demographics and test results, Democratic Republic of Congo, 2013-2014

	Test results			
Sociodemographic characteristic	Positive	Negative	Indeterminate	Children age 6-59 months with a test result
Sex				
Male	62.9	34.4	2.8	4,074
Female	66.0	31.9	2.1	4,043
Age category (in months)				
6-8	18.3	81.1	0.6	414
9-11	40.9	57.2	1.9	463
12-23	54.3	42.9	2.8	1,767
12-17	*51.0*	*46.7*	*2.3*	*998*
18-23	*58.6*	*37.9*	*3.5*	*769*
24-35	66.5	32.1	1.3	1,851
36-47	74.8	22.0	3.2	1,792
48-59	78.4	18.5	3.0	1,830
Place of residence				
Urban	65.3	32.9	1.9	2,417
Rural	64.1	33.2	2.7	5,700
Province				
Kinshasa	75.8	22.5	1.7	535
Bas-Congo	59.3	37.2	3.4	338
Bandundu	59.8	39.0	1.2	1,336
Équateur	72.8	24.8	2.4	1,253
Orientale	76.0	21.2	2.7	806
Nord-Kivu	81.6	16.2	2.2	653
Sud-Kivu	69.4	26.5	4.0	593
Maniema	52.0	43.3	4.7	283
Katanga	51.4	46.5	2.1	835
Kasaï Oriental	51.9	45.9	2.2	875
Kasaï Occidental	53.6	43.1	3.4	609
Total	**64.4**	**33.1**	**2.4**	**8,116**

Example 12: In this 2002 study from the region of Catalonia in Spain, representative samples of children and adults were used to estimate the seroprevalence of antibodies against measles, mumps, and rubella in children five years and older and adults of all ages. Based on this data, the author recommended MMR vaccination for susceptible children aged 5-14 years and adolescents/young adults age 15-24, identified using pre-vaccination screening.

Reference: Plans P. New preventive strategy to eliminate measles, mumps, and rubella from Europe based on the serological assessment of herd immunity levels in the population. Eur J Clin Microbiol Infect Dis. 2013 Jul;32(7):961-966.

Age (years)	Prevalence of positive serological results (p)						
	Measles		Mumps		Rubella		
	%	95 % CI	%	95 % CI	%	95 % CI	n
5–9	85.5	80.7–90.3	83.3	78.3–88.4	98.2	95.6–99.5	228
10–14	93.3	91.8–94.9	89.1	87.2–91.0	93.3	91.8–94.9	1,096
15–24	83.8	77.2–90.4	89.0	83.3–94.6	97.1	92.6–99.2	136
25–29	90.5	84.8–96.3	87.9	81.6–94.3	98.3	93.9–99.8	116
30–34	98.1	93.3–99.8	91.5	85.7–97.3	100.0	–	106
35–39	97.7	94.3–99.5	89.3	83.6–95.0	97.7	93.4–99.5	131
40–44	96.3	91.6–98.8	90.4	85.1–95.7	97.8	93.7–99.5	130
45–49	97.9	94.0–99.6	88.1	82.5–93.8	97.9	94.0–99.5	143
50–54	98.5	94.7–99.8	94.7	90.6–98.9	97.7	93.5–99.5	133
55–59	100.0	–	92.9	88.1–97.8	98.4	94.4–99.8	127
60–64	98.0	92.9–99.7	97.0	91.4–99.4	99.0	94.5–100	99
65–69	100.0	–	91.3	85.0–97.6	100.0	–	92
>69	100.0	–	92.1	85.4–98.8	100.0	–	76
Total 5–14[c]	89.5	87.8–91.1	86.3	84.5–88.2	95.7	94.6–96.8	1,324
Total ≥15[c]	96.1	95.0–97.1	91.1	89.6–92.7	98.1	97.3–98.8	1,295

WHO Measles Strategic Planning (MSP) Tool and Other Excel-Based Tools

Example 13: The example below shows a baseline immunity profile for children 0-14 years in 2008 in Kenya generated by the MSP tool. This takes into account their historical coverage, SIAs, population and surveillance data that was entered into the tool. It estimates that ~30% of children 3 years and younger were susceptible to measles, as these birth cohorts had not yet been exposed to an SIA. The estimated immunity in older cohorts was close to 100%, with 60-70% of the children immune due to routine immunization and 30-40% protected by SIAs.

Reference: Simons E, et al. Strategic planning for measles control: using data to inform optimal vaccination strategies. J Infect Dis. 2011 Jul;204 Suppl 1:S28–S34.

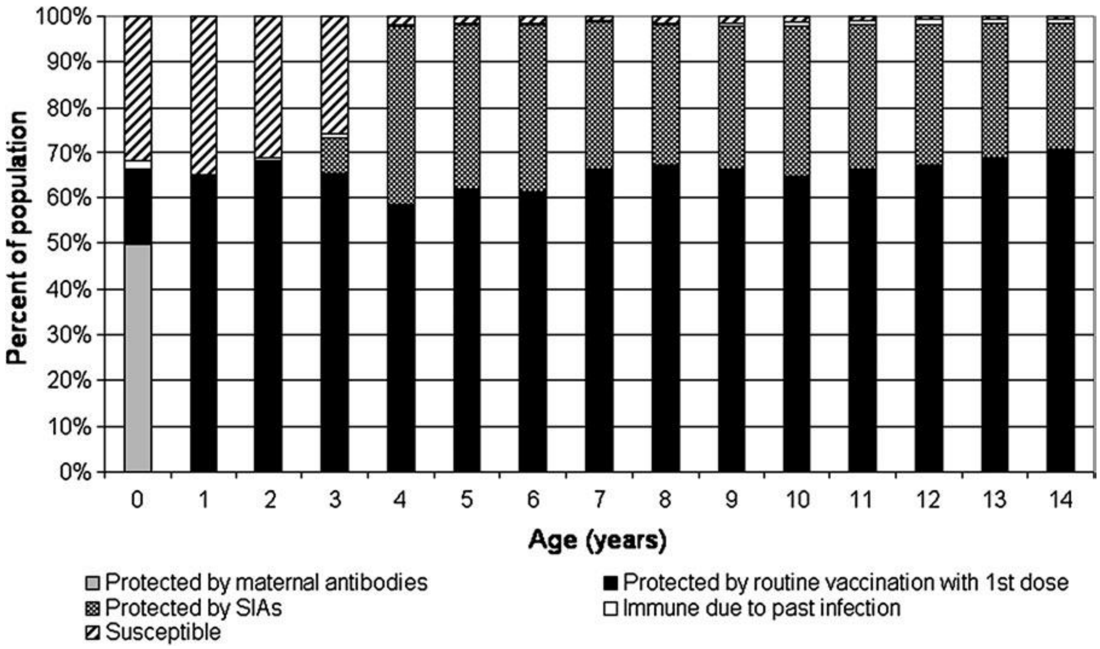


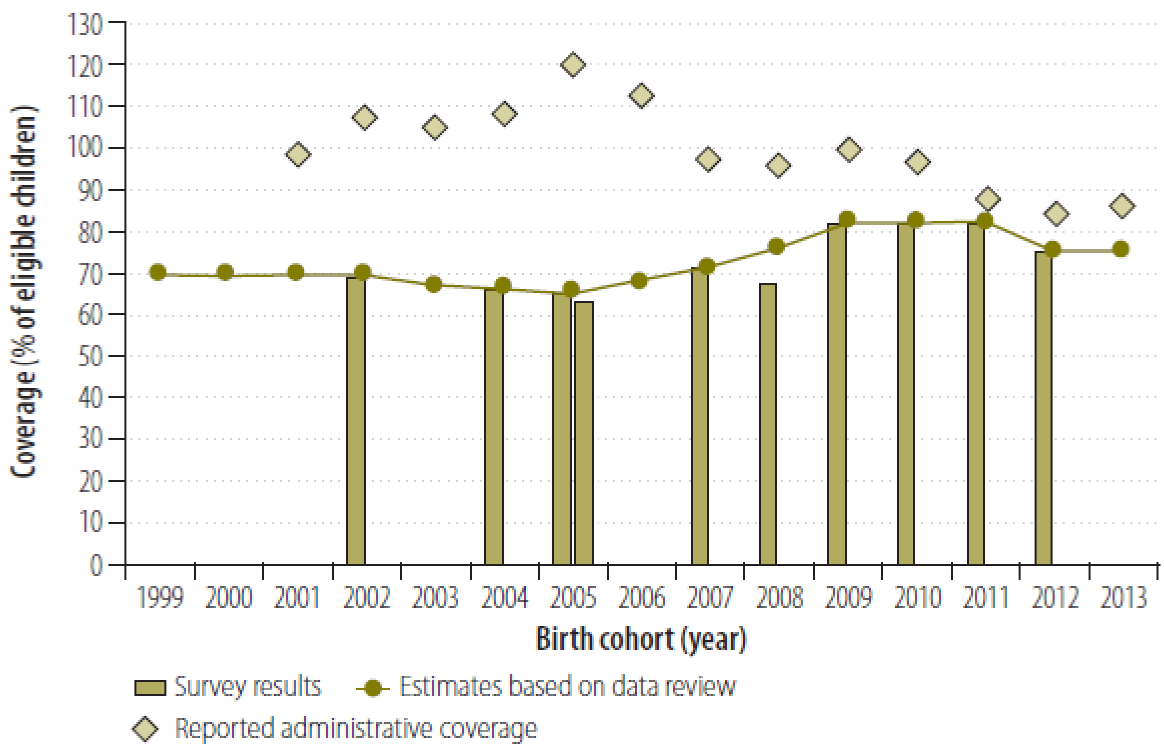
Figure 4. Population immunity and infection profile for children 0–14 years in 2008 in Kenya.

Data Triangulation

Example 14: In this example from India, they triangulated all available administrative and coverage data, taking into account the reliability of each estimate and using methodology based on WUENIC methodology. This included consideration of things that may have affected coverage like stock outs and a comparison of data across different vaccines to look for inconsistencies. Estimates were generated for 17 states and then combined into a national estimate to provide both national and state-level estimates. Comparison of all available data sources allowed the country to make estimates that are likely to be more accurate than their reported administrative coverage.

Reference: Bhatnagar P, et al. Estimation of child vaccination coverage at state and national levels in India. Bull World Health Organ. 2016 Oct;94(10):728-734.

Fig. 1. **Estimates of the coverage for routine child immunization with the third dose of vaccine against diphtheria, tetanus and pertussis in the state of Chhattisgarh, India, 1999–2013**



Notes: The three different sets of estimates that are shown are based on the data review described in this article, reported administrative coverage and surveys for the evaluation of coverage. The absence of a bar for a particular cohort indicates the absence of relevant survey data – and not that a survey indicated zero coverage of that cohort.

Example 15: In their paper "Approach to Verify the Status of Measles, Rubella and Congenital Rubella Syndrome Elimination in Costa Rica" (J Infect Dis, 2011), Morice et al describe their approach to estimate population immunity using multiple sources of data during the process of measles and rubella elimination verification:

"Population cohorts vaccinated since 1986, the year the MMR vaccine was introduced in the routine schedule, were analyzed. The proportion of the 1- to 40-year-old population in 2007 that had been vaccinated was estimated for both sexes. The source of the data was the Ministry of Health report on administrative coverage of the various immunization strategies, by year of birth and target group, including the routine schedule (aged 1 year, beginning in 1996); the catch-up campaign aged 1-14, in 1993); mop-up campaigns (aged 1-4, in 1994, 1997, and 2002); the campaign to vaccinate adolescents and adults (aged 15-39, in 2001); and postpartum vaccination (pregnant women aged 15-39, May 2001 to February 2002).

The quality of the administrative coverage data for the routine program was confirmed by analyzing consistency both with the results of vaccination coverage surveys conducted in 2002, 2006, and 2010, through the inclusion of a module in the National Multipurpose Household Survey, and with seroprevalence studies reported in the country.

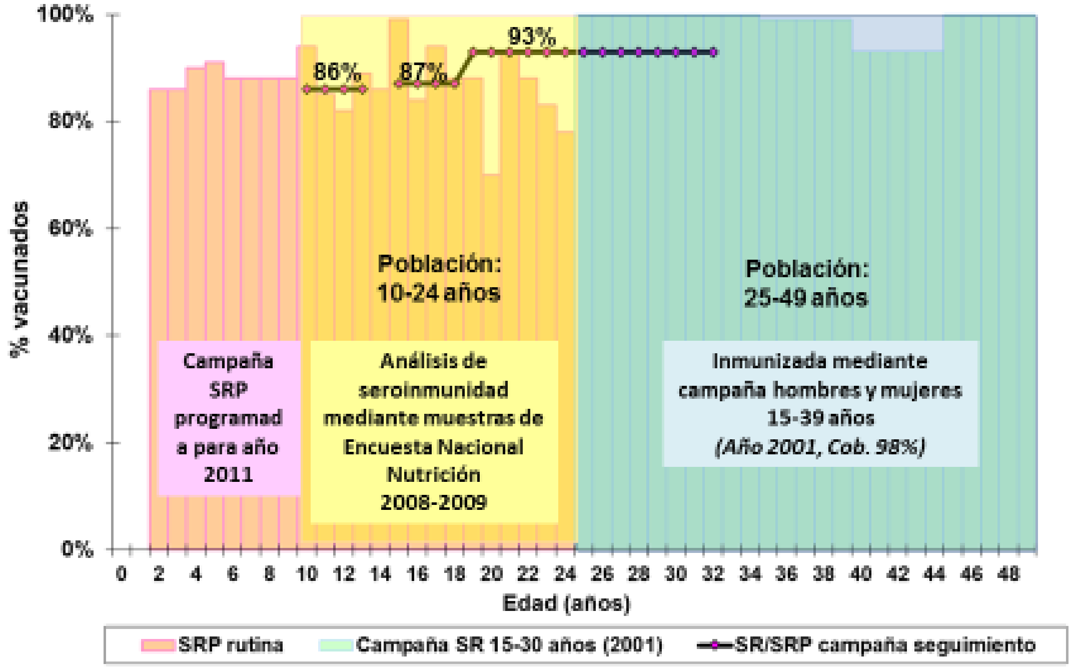
Another source of information used to evaluate vaccination coverage was the vaccination registry maintained by the Costa Rican Social Security Fund; unvaccinated children can be identified by associating the universally issued birth identification number with records of the doses of MR/MMR administered. To verify rubella seroimmunity level in the population aged 10-24 years, we processed the serum samples taken in this group of age during 2008-2009 for the National Nutritional Household Survey in Costa Rica."

This figure shows Costa Rica's immunity profile for persons age 1-49 in 2011 based on the methods described above. The green bars show age cohorts vaccinated in a 2001 campaign, which achieved 98% coverage. The dotted lines show coverage in the cohorts vaccinated during 3 SIAs. The orange and yellow bars show coverage through routine immunization. The yellow background shows results from a 2008-2009 serosurvey, which indicated that 98.6% of persons in those age cohorts were seropositive. The gap in immunity among children under 10 years old was to be addressed through an SIA targeting children 1-9 years old in 2001.

References:

1) Morice A, et al. Approach to verify the status of measles, rubella and congenital rubella syndrome elimination in Costa Rica. J Infect Dis. 2011 Sep;204 Supply2:S690-697. (Text)
2) Faingezitch, Idris. Avances, retos y oportunidades para documentar la eliminacion del sarampion, rubeola y SRC. La experiencia de Costa Rica. Presented at the: Reunion de Comité Internacional de Expertos y Comisiones Nacionales para Documentar y Verificar la Eliminacion del Sarampion, Rubeola y SRC. (Figure)

Estimación de cohortes de 0 a 49 años de edad población vacunada con SR/SRP utilizando estrategias combinadas de inmunizacion. Costa Rica, 2011



Fuente: Ministerio de Salud de Costa Rica, Dirección de Vigilancia

Mathematical Modeling

Example 16: This model predicts measles immunity in the presence or absence of SIA campaigns using data from Lusaka, Zambia. In children <5 years, immunity to measles is estimated at 68% without an SIA and with current routine coverage; immunity increases to 81% with the addition of an RI 2nd dose. The model predicts that more frequent, lower coverage SIAs will keep all-age population immunity higher than less frequent, higher coverage SIAs.

Reference: Lessler J, et al. Maintaining high rates of measles immunization in Africa. Epidemiol Infect. 2011 Jul;139(7):1039-1049.

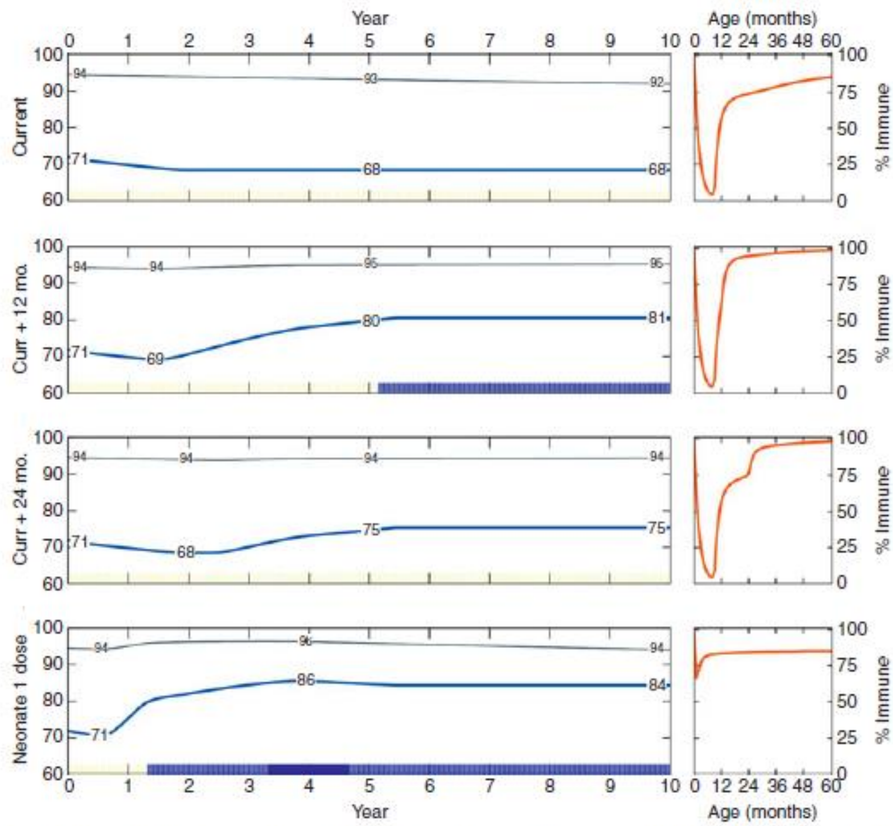


Fig. 3. Predicted levels of immunity achieved by differing measles vaccination schedules. The left panels show the percentage aged <5 years (thick blue line) and the entire population (thin grey line) predicted to be immune to measles in the absence of circulating virus for 10 years after instituting the given vaccination programme. The right panels show the percentage of children aged 0–60 months predicted to be immune to measles by age after the given programme has been in place for 10 years.

Example 17: This paper uses a model to estimate age-specific residual susceptibility based on historical serological data for 9 countries with a range of SES. The model finds that in high-income countries, approximately 20% of susceptible individuals are <5 years; in low-income high-fertility countries, up to 60% of susceptible individuals are <10 years and up to 40% are <5 years.

Reference: Trentini F, et al. Measles immunity gaps and the progress towards elimination: a multi-country modelling analysis. Lancet Infect Dis. 2017 Oct;17(10):1089-1097.

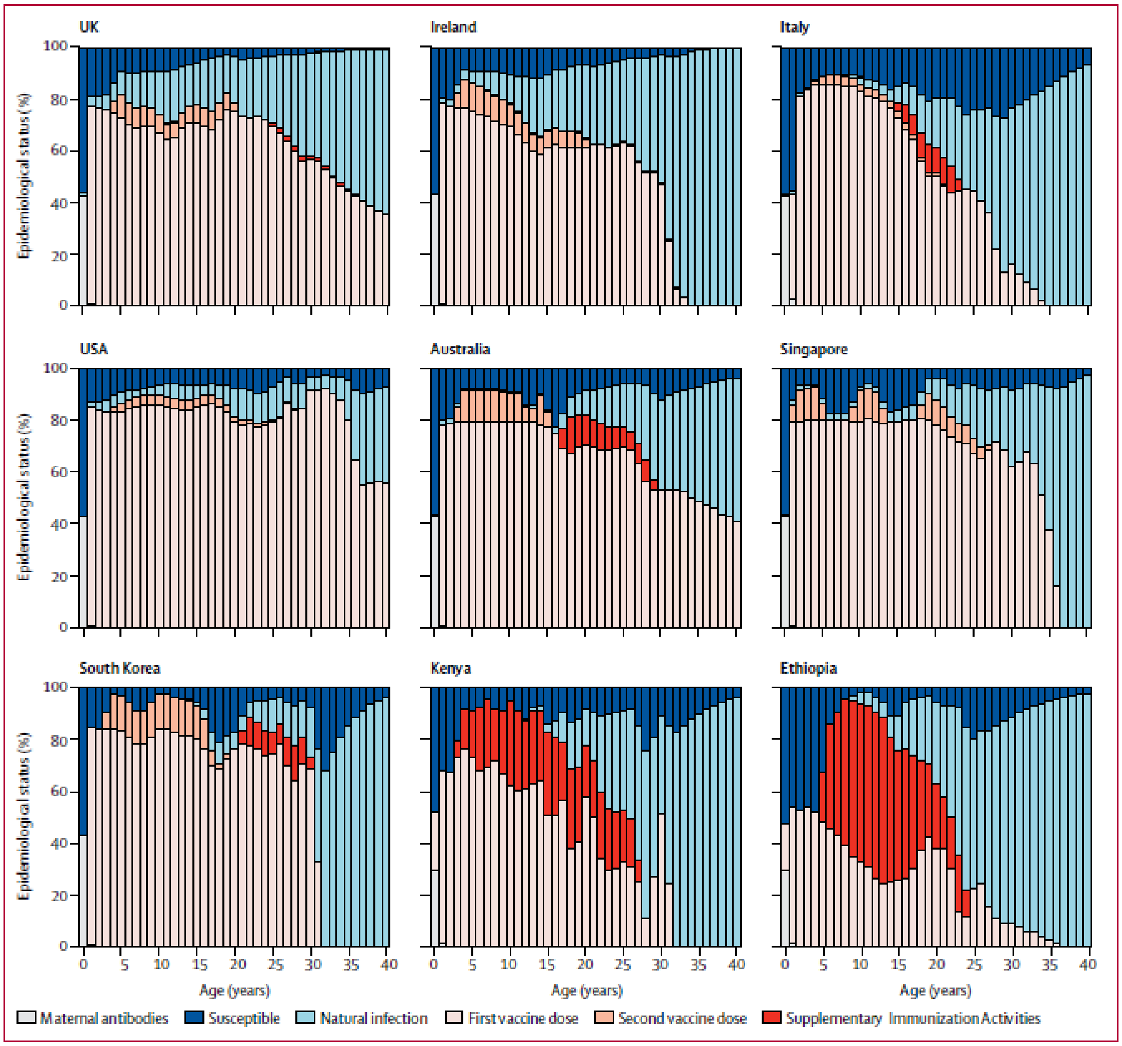


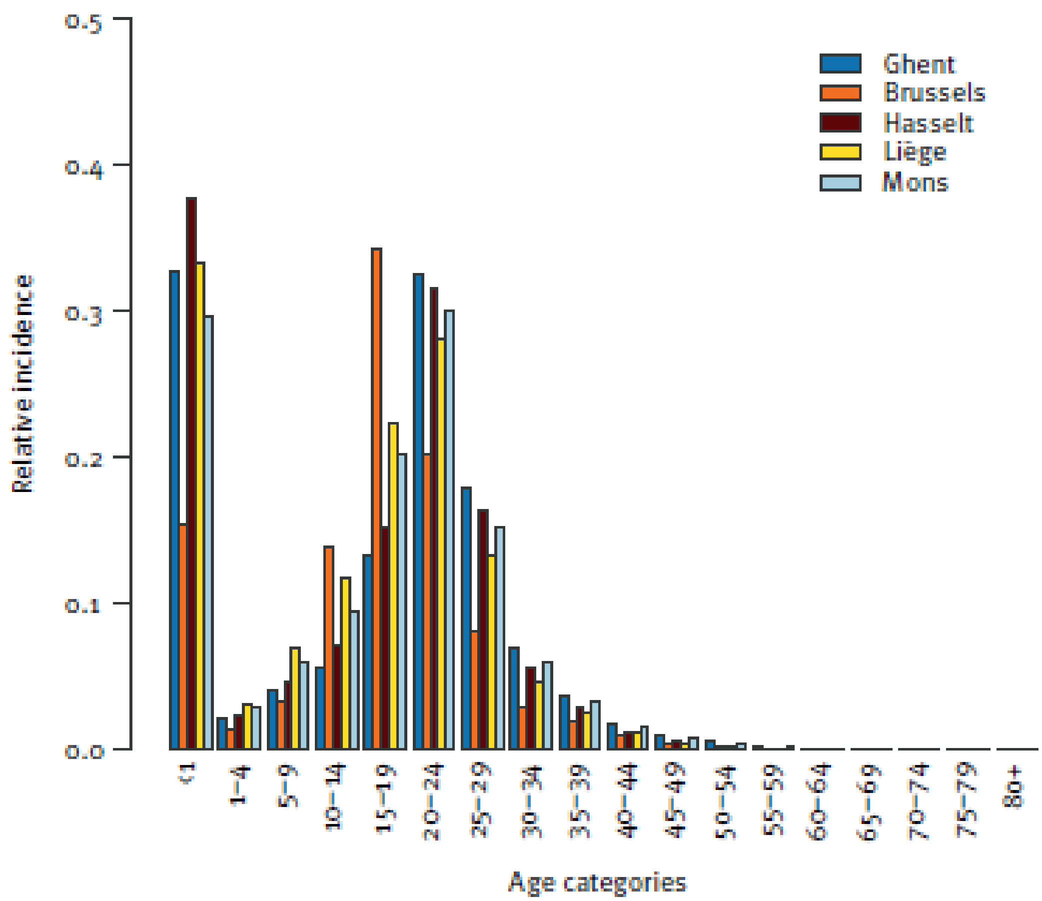
Figure 4: **Estimated immunity profiles**
Model estimates of the epidemiological status at different ages and in different countries for 2015. Shown for each age stratum is the percentage of individuals susceptible to infection or protected against infection by immunity provided by maternal antibodies and by immunity acquired through natural infection, routine first-dose vaccination, second booster administration, or Supplementary Immunization Activities.

Example 18: This multi-cohort model uses historical spatial sero-survey data, vaccination coverage data, and social contacts data, and was applied to five Belgian cities to estimate expected age-specific measles incidence. It predicted highest incidence among infants <1 year, adolescents 15-19 years, and young adults 20-29 years.

Reference: Hens N, et al. Assessing the risk of measles resurgence in a highly vaccinated population: Belgium anno 2013. Euro Surveill. 2015 Jan;20(1).

FIGURE 4

Predicted age-specific relative incidence for newly emerging measles outbreaks in five Belgian cities: Brussels, Ghent, Hasselt, Liège and Mons, 2013



Example 19: This paper uses mathematical models to estimate age-specific susceptibility to rubella virus infection based on calculations using pre-RCV rubella seroprevalence estimates, estimated vaccination coverage in the routine schedule and mass campaigns.

Reference: Vynnycky E, et al. Using Seroprevalence and Immunisation Coverage Data to Estimate the Global Burden of Congenital Rubella Syndrome, 1996-2010: A Systematic Review. PLoS One. 2016 Mar 10;11(3):e0149160.

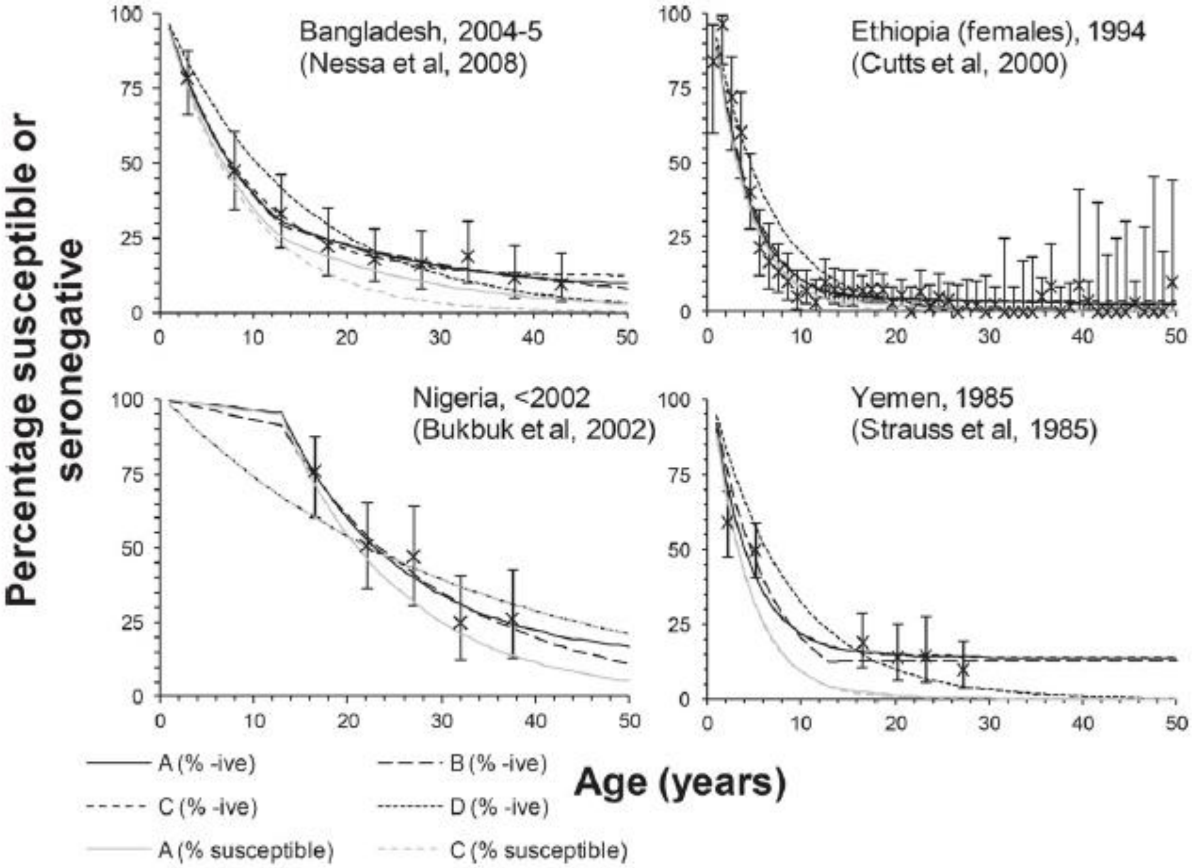


Fig 2. Examples of the fit of catalytic models to the data sets. Comparison between model predictions of the percentage susceptible and the percentage seronegative to rubella obtained using the four types of catalytic model (denoted by the lines labelled A, B, C and D), and that observed in various settings. The crosses show the observed percentage seronegative together with 95% (exact) confidence intervals.

doi:10.1371/journal.pone.0149160.g002

Example 20: This model uses Demographic and Health Surveys and generalized additive models to quantify spatial patterns of measles vaccination in ten contiguous countries in the African Great Lakes region during 2009-2014. The model shows that over 14 million children <5 years of age live in 'coldspots' where vaccine coverage is below the WHO target of 80%, and a total of 8–12 million children are unvaccinated. This clustering of low vaccination areas allows for pockets of susceptibility that could sustain circulation despite high overall coverage.

Reference: Takahashi S, et al. The geography of measles vaccination in the African Great Lakes region. Nat Commun. 2017 May;8:15585.

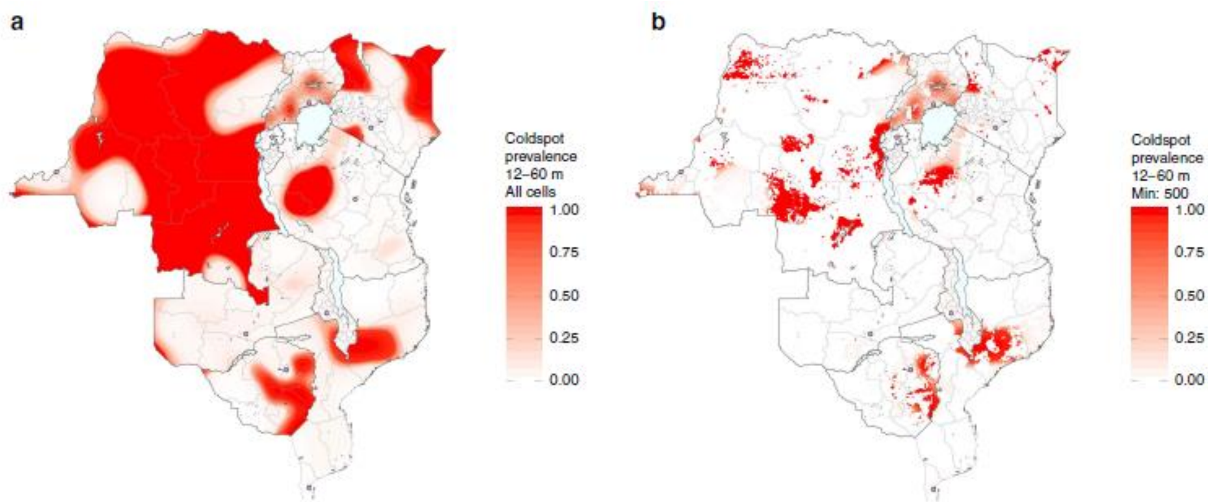


Figure 3 | Vaccination coldspots and population density. Estimated proportion of monthly age cohorts that each 10 km by 10 km grid cell exists as a coldspot of routine and national SIA measles vaccination for children between 12–60 months of age (total of 49 monthly age cohorts), showing (**a**) all grid cells (long-term coldspots) and (**b**) only grid cells with at least 500 children under 60 months of age (long-term, high-density coldspots). Capital cities are shown as pink circles. The first sub-national political boundaries are shown in light grey.