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The seroepidemiology of measles in Western Europe

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SUMMARY

The European Regional Office of WHO has targeted measles for elimination from the region in 2007. Large national, age and sex stratified serological surveys of measles antibody were conducted in seven Western European countries from 1994–8 as part of the European Sero-epidemiology Network. Three patterns were observed in the country-specific measles seroprofiles, ranging from (very) low susceptibility (four countries) to high susceptibility (one country). Susceptibility levels amongst 2–4-year-olds ranged from 2·9 to 29·8%, in 5–9-year-olds from 2·5 to 25% and 10–19-year-olds from 2·1% to 13·9%. A country's susceptibility profile was highly associated with vaccine coverage for the first dose. First dose coverage ranged from 91 to 97·5% for low susceptibility countries, 75 to 85% for intermediate susceptibility countries and 55% for the high susceptibility country. Only the high susceptibility country still reports epidemic measles. In low susceptibility countries, which have achieved or are very close to measles elimination, the priority will be to maintain high MMR vaccine coverage in all geopolitical units for both vaccine doses. In moderate susceptibility countries

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there is still some endemic transmission, but also risk of outbreaks as pools of susceptibles accumulate. In the high susceptibility country the priority will be to increase infant vaccine coverage and reduce regional variation in coverage levels.

INTRODUCTION

Measles is an acute viral infection of very high transmissibility, which resulted in almost universal infection during early childhood in the pre-immunization era [1]. Due to the availability of a highly efficacious vaccine for over 30 years, the implementation of measles control programmes has been a very cost-effective intervention in both developing and developed countries [2] and many countries have now moved from a control to an elimination phase [3]. The WHO Regional Office has targeted measles for elimination from Europe by year 2007 [4].

A variety of vaccination strategies have and are being used in an attempt to interrupt transmission, including two-dose vaccination programmes and a one-dose programme with catch-up campaigns [5]. The success of a vaccine programme, especially moving from the control to the elimination phase, requires the identification of susceptible age groups. This depends upon high quality measles surveillance data, including accurate age-specific incidence data and measles vaccine coverage levels. Population-based serological surveys measure the population susceptibility profile, providing a more direct measure of a vaccination programme's impact. The age-group specific susceptibility levels needed to achieve measles control in Europe have now been established [6].

To determine if these susceptibility targets have been reached, comparability of serosurvey results is essential. Internationally, a variety of serological methods have been used to collect sera and measure measles antibody levels. The European Sero-Epidemiology Network (ESEN) was established to coordinate and harmonize the serological surveillance of immunity to several vaccine preventable diseases including measles [7]. We present the standardized results of national serological surveys from seven Western European countries performed with comparable designs, providing a unique opportunity not only to compare the serological and epidemiological impact of a variety of measles vaccination schedules and coverage levels, but also to assess progress towards measles control and elimination in Western Europe.

METHODS

Serum survey collection

Seven of the member countries of ESEN undertook collection and testing of several thousand sera specimens between 1994 and 1998 (Denmark, England and Wales, Finland, France, Germany, Italy, The Netherlands). In Denmark, sera collection for those less than 6 years was undertaken in 1997–8, those aged 6–16 years was performed in 1994. The minimum number of sera to collect per age group was determined from power calculations using age specific estimates of seroprevalence of antibody to various vaccine preventable infections. The number of sera collected per country ranged from 2766–8303.

The sources of sera used have been described previously [8]. Two methods of sampling were used: population based random sampling and use of residual sera collected during routine laboratory testing. In both cases, samples were collected from a variety of geographical locations within each country to provide a reasonably representative estimate of the general population immunity. For each specimen, the age, sex and year of collection were gathered plus some regional data in Italy (North and South) and Germany (East and West). The sole exclusion criterion was sera collected from individuals with known immune deficiencies.

Standardization: panel distribution and testing

To achieve quantitative comparability of assay results between countries, the results of measles antibody testing were standardized using a methodology developed as part of the ESEN project. This has been described in detail previously [9]. Briefly, the process involved the distribution of a panel of 150 negative, low positive and positive sera for measles antibody by a reference laboratory (Statens Serum Institut, Copenhagen, Denmark) to the national laboratory in each participating country. The panel was tested in each national laboratory by their usual quantitative enzyme immunoassay (EIA). Standardization equations were calculated by regressing the local results of panel testing in these countries against those of the reference laboratory.

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Table 1. *Age-specific percentage of seronegativity for measles antibody in seven countries of ESEN and WHO target*

Country	2–4 years	5–9 years	10–19 years	20–39 years	> = 40 years
WHO Target	< 15%	< 10%	< 5%	< 5%	< 5%
Low susceptibility					
FI	2·9%	2·5%	2·1%	1·4%	0·3%
NL	4·0%	4·7%	5·1%	1·8%	0·1%
UK	14%	8·8%	4·7%	5·1%	3·3%
FR	10·3%	9·9%	5·0%	1·2%	0·2%
Intermediate susceptibility					
DK	24·2%	10·5%	4·7%	0·5%	0·5%
DE	23·1%	9·1%	7·5%	2·0%	0·5%
High susceptibility					
IT	29·8%	25·0%	13·9%	4·3%	1·3%

Main serum survey testing

The main national serum survey was tested using the same validated assay method. The country-specific standardization equations were used to convert the local quantitative results of the serum survey into standardized reference laboratory unitage. The reference laboratory cut-off range (the EIA of Behring assay) was used to classify these standardized quantitative results as positive, low positive or negative (negative < 150 mI U; low positive 150–350 mI U; positive > 350 mI U). Unless otherwise stated, the low positives were reclassified as positive.

As detailed in a paper describing the standardization process, these values are at variance with the unitages produced by other EIAs [9], thus the results reported in this paper may differ slightly from percentages reported elsewhere by individual countries.

Vaccine programme structure and coverage

A questionnaire was distributed to all participating countries to gather data on measles vaccine programme organisation, historical vaccine coverage and age-specific incidence of measles. Some of these results have previously been reported [5].

Coverage estimation

A number of countries had inadequate or incomplete coverage data on their vaccination programmes. Estimates of the level of MMR vaccine coverage in each country were derived from the ESEN serological data [10]. This method utilises serological data at the individual level to estimate the proportion of individuals of a given age who have been vaccinated and the proportion infected with each of the three viruses. By assuming that seroconversion to each of the three antigens is independent within an individual and that the viruses circulate independently of each other (so the chances of being infected are independent), then the probability of an individual of a given age being in any of the eight mutually exclusive serological groups (ranging from positive to all three to negative to all three) can be described in terms of vaccine coverage (in that cohort), vaccine efficacy for each of the three components of the vaccine, and the cumulative infection rates. These parameters are then estimated using maximum likelihood. Estimates of monovalent measles vaccine coverage prior to the introduction of MMR were made from official statistics or by questionnaire distributed to the ESEN country co-ordinators [5].

RESULTS

Three patterns were observed in the country-specific measles seroprofiles based on the WHO Regional Office for Europe age-specific susceptibility levels recommended to interrupt measles transmission (Table 1; Appendix). These patterns ranged from low susceptibility to high susceptibility. In none of the seven countries was a significant sex difference observed in the proportion seronegative in any of the age groups (data not shown). For all countries, the proportion of low positives was highest in those age-cohorts in whom a large proportion were vaccinated at least a few years ago (Fig. 1).

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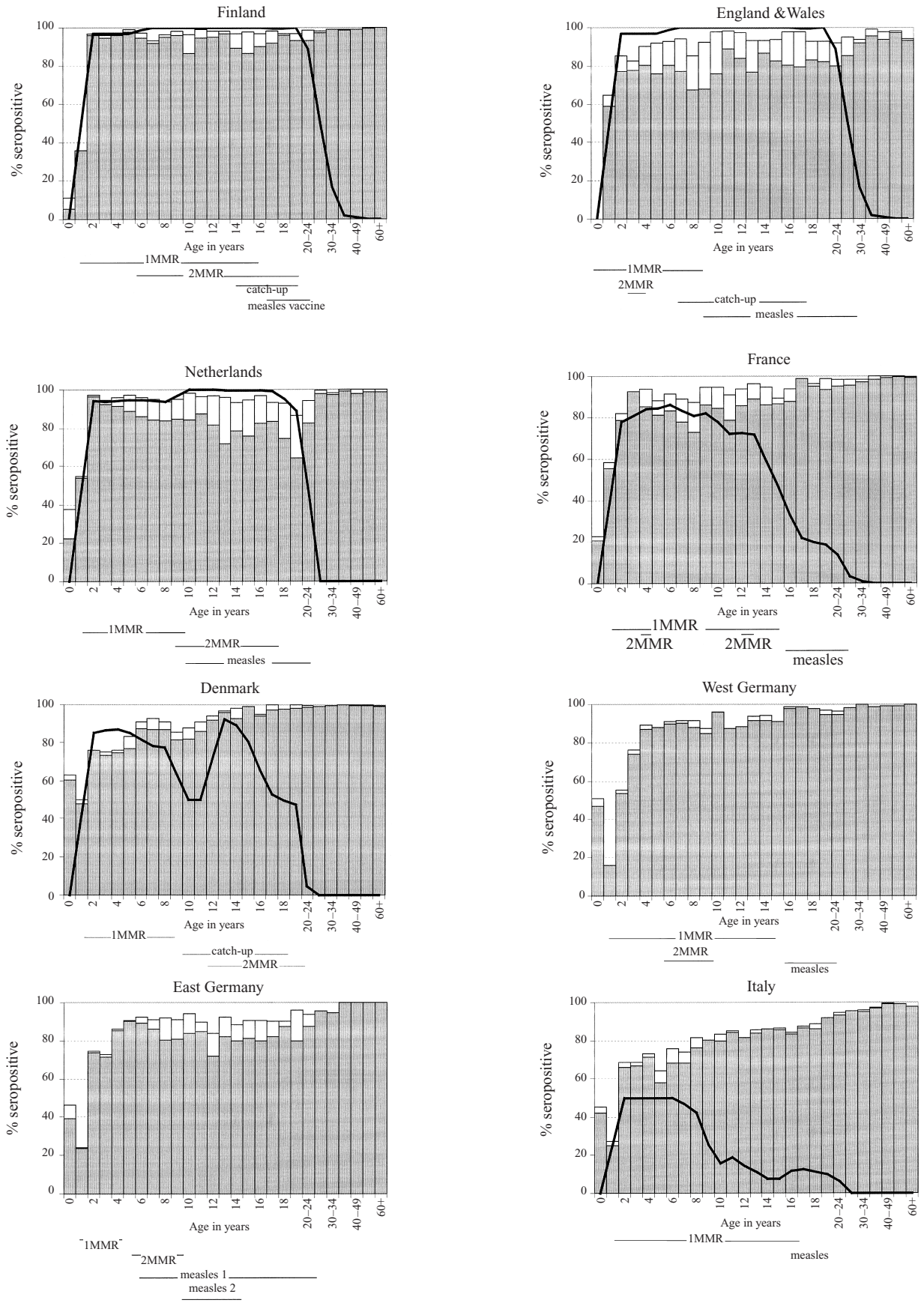

Fig. 1. For legend see facing page.

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Low susceptibility countries

The group with low susceptibility includes Finland, The Netherlands, France and England and Wales.

Table 1 shows that for Finland and The Netherlands, the age-specific susceptibility levels are well below the WHO target levels, further illustrated by their respective age specific population seroprofiles (Fig. 1). These figures show the proportion in each age class with measles antibody (seropositive and equivocal) and the proportion estimated to have vaccine derived immunity. Below the figure the vaccine programme in place for each age-cohort is shown. In both countries, the proportion seronegative in any agegroup (particularly in 1–20-year-olds) does not exceed 5% (except 5·1% for 10–19-year-olds in The Netherlands). In Finland, the proportion seronegative is even lower than in The Netherlands (Table 1). Virtually all those seropositive for measles antibody under 20 years of age are estimated to have vaccine derived immunity (Fig. 1). This is a reflection of the introduction of measles vaccine approximately 25 years ago, followed by a two-dose MMR programmes with very high coverage in both countries in the early 1980s. Reported vaccine coverage has been slightly higher (97% for both doses) in Finland compared to The Netherlands (94% for the first dose and estimated to be similar for the second dose). Finland in addition undertook a catch-up campaign targeted at 2–6-year-olds, when the MMR programme was initially introduced. Both countries from the serosurvey seem to be apparently near the elimination of measles. In Finland and until recently The Netherlands (see later), there has been an extremely low reported incidence of confirmed clinical cases (Fig. 2).

The United Kingdom and France have recently joined the low susceptibility countries. The population susceptibility levels are higher then those in The Netherlands and Finland and only just within the WHO recommended targets (Table 1). The majority of seropositives under the age of 18 years at the time of the serosurvey in the United Kingdom are estimated to have vaccine-derived immunity (Fig. 1). This is a reflection of the vaccination programme history: single dose MMR vaccine was introduced in 1988, with reported vaccine coverage increasing from 80% to around 90% only recently. However, a mass measles-rubella catch-up campaign was conducted in November 1994 targeted at 5–16-year-olds (with reported 92% coverage), and a second dose of MMR introduced at the end of 1996 for 4-year-olds. The reported incidence of clinical measles fell below 10/100000 in 1996 (Fig. 2), although only a small proportion (10%) of these rash-illness cases are laboratory confirmed as measles cases [11].

For France, the serological profile resembles that of the United Kingdom. The seronegativity level amongst 2–9-year-olds is about 10% and 5% for 10–19-year-olds (Table 1). France introduced a single dose MMR vaccination in 1983. A second dose was introduced in 1996 initially for 11–13-year-olds and then changed to 3–6-year-olds the following year (Fig. 1). Measles epidemic cycles have been interrupted in France since 1987. The incidence rate of measles estimated from a network of sentinel GPs, had levelled at approximately 100/100000 inhabitants between 1993 and 1997, and has fallen down to 32/100000 population in 1998 (Fig. 2).

Intermediate susceptibility countries

The group with intermediate susceptibility includes Denmark and Germany, as in both these countries, susceptibility levels are not within the WHO targets.

In Denmark, no measles vaccination (either with MMR or single antigen measles vaccine) occurred until 1987. A two-dose MMR vaccination programme was introduced in this year (at age 15 months and 12 years). A catch-up targeted at children aged 2–10 years was also conducted at this time. From the serological survey, 24% of 2–4-year-olds remain seronegative and 10% of 5–9-year-olds (Table 1). This falls to below 5% for 10–19-years-olds. Virtually all those who are seropositive under 5 years of age, probably acquired immunity through vaccination (Fig. 1). A large proportion of 5–12-year-olds were naturally infected, with an increase in the proportion with vaccine derived immunity at 13 years of age with the second dose of MMR. We do not know what proportion of these had already experienced natural infection earlier in life. Epidemic transmission has been interrupted and the reported measles incidence has been below 3/100000 since 1992 (Fig. 2).

Germany is the other intermediate susceptibility

Fig. 1. Seroprevalence of measles antibody for each ESEN member country (■ antibody positive, □ low antibody positive), the estimated proportion of each age-group vaccinated (—) and their vaccine history by age-group (in years). Age-group vaccine history defined below each figure: measles, MMR1 (single dose mass infant vaccination programme), MMR2 (second dose mass vaccination programme), catch-up (one-off targeted vaccination programme).

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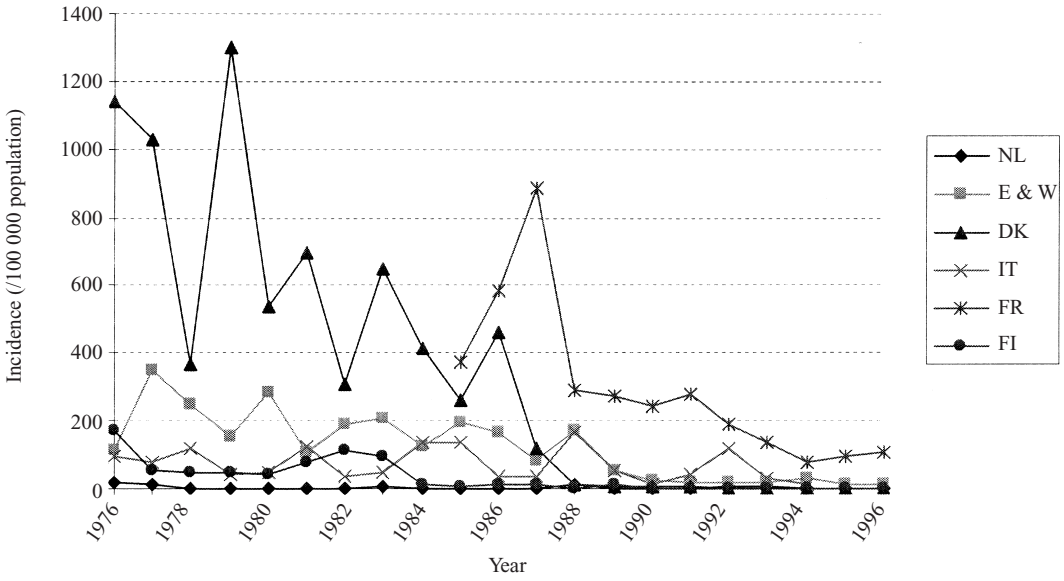

Fig. 2. Reported incidence of measles infection per 100000 population in six ESEN countries.

country (Table 1). The serological survey shows that a high proportion of 2–4-year-olds are seronegative and a higher proportion of 10–19-year-olds compared to Denmark (Table 1). There is also a significant difference in the age-specific seropositivity between sera taken from former East and West Germany (Fig. 1). The vaccination programme history differs between the Eastern and Western parts of the country. In West Germany, recommendations for measles vaccination were introduced in 1975, followed by single dose MMR vaccination in 1980. In East Germany, compulsory infant monovalent measles vaccination was started in 1970, followed by a monovalent two-dose strategy in 1986. The reported coverage in the former GDR was > 95%, whereas the estimated coverage in West Germany was only 60–80%. After re-unification in 1991, a two-dose MMR vaccination programme was recommended throughout Germany, with the second dose for 6-year-olds. No data are available on the incidence of measles infection in Germany.

High susceptibility countries

Italy is the only country belonging to the high susceptibility group. The proportion seronegative amongst 2–4-year-olds and 5–9-year-olds is approximately 30 and 15% in 10–19-year-olds, considerably higher than the low and intermediate susceptibility countries (Table 1). Fifty percent of children aged 2–6 years were estimated to have vaccine derived immunity in 1996, although a large proportion even in the younger age-classes probably acquired immunity through exposure to wild virus (Fig. 1). Voluntary vaccination with one dose of MMR was introduced in 1979 and there are large reported regional differences in coverage (ranging from 26–88% from the South to North) [12], although there was no significant difference in the seroprofile by region (data not shown). Indeed, measles still remains epidemic in Italy, with regular 4-yearly epidemic cycles reported (Fig. 2).

DISCUSSION

ESEN is the first study to our knowledge to present comparable results of population-based measles sero-surveillance studies from several countries, with all participants having undertaken collections of large samples of sera, tested with standardized methodology.

The study confirms that high vaccine coverage is the most important factor needed to interrupt and control measles transmission. A country's susceptibility profile was highly associated with vaccine coverage for the first dose. With the exception of Denmark, the susceptibility level was directly associated with the reported incidence of measles [5]. Both Finland and The Netherlands have had high vaccine coverage for over 10 years, with an interruption of epidemic measles, so virtually no immunity in the younger age groups is naturally acquired and all is vaccine derived. Finland has moved from the control to the elimination phase with no serologically confirmed measles cases

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identified since 1996 [13, 14]. In The Netherlands the annual number of notified measles cases has decreased from 472 (3·1/100000) to 57 (0·37/100000) over the period 1992–6 [15]. Factors besides the slightly lower vaccine coverage to explain this continued measles circulation in The Netherlands could include the more elaborate catch-up conducted in Finland, more importation of measles virus in The Netherlands and circulation of wild virus in the clusters of religious groups who refuse vaccination. Indeed, in 1999–2000, an outbreak of measles occurred in The Netherlands with almost 3000 cases and 3 measles related deaths. The outbreak started in a school where most children were not vaccinated for religious reasons, and spread to religious groups around the country who refrain from vaccination [16].

Other countries, such as the United Kingdom and France, have recently undertaken specific interventions to improve vaccine programme performance and thus move from the intermediate to the low susceptibility group. In the United Kingdom, coverage with single-dose monovalent measles vaccine prior to 1988 was only adequate to reduce the incidence of measles infection, but not to immunize all of each birth cohort. After, a period of time, susceptibles had accumulated amongst older age groups. With predictions of a measles epidemic, a national catch-up campaign was conducted in November 1994 targeted at 5–16-year-olds [17], followed by the introduction of a second dose of MMR in 1996. Unfortunately, routine vaccine coverage levels in the United Kingdom have not been maintained due to some public concern over vaccine safety. In France, modelling undertaken through the ESEN project showed the likelihood of a large outbreak of measles in the younger age-groups without an increase in vaccination coverage or a catch-up campaign. Thus the low susceptibility observed in the 2–4-year-olds most likely reflects this recent catch-up following a media campaign in mid-1997 together with a simultaneous lowering of the age of the second dose to between 3 and 6 years. However, available data show that routine vaccination coverage of children under 2 years of age has not increased. Thus France's position as a low susceptibility country is also a little misleading, as current levels of vaccine coverage will result in a re-accumulation of susceptibles.

The intermediate susceptibility countries include Denmark and Germany. The low incidence of notified measles in Denmark compared to the relatively high level of susceptibility in under-10-year-olds suggests a honeymoon phase (or alternatively important under-notification). This term describes the period after the introduction of mass vaccination with moderate coverage during which disease incidence is low. As coverage levels are only moderate, there is an accumulation of susceptibles over time, until the epidemic threshold is surpassed and an outbreak occurs. A catch-up campaign in conjunction with improved coverage of both the first and second doses would prevent this phenomenon. In Germany, the gradual decrease in seronegativity observed between the age of 2 and 5 years is probably due to several factors: the impact of second dose MMR introduced in 1991; closing vaccination gaps during the legal medical examination before school entry of 6-year-old children and natural infection as occurred during the epidemic outbreak in 1996 [10, 18]. Unfortunately, the lack of corroborating evidence regarding coverage and the absence of measles surveillance data hampers further investigation.

The low vaccine coverage in Italy has reduced, but not completely stopped viral circulation amongst infants, resulting in the accumulation of a pool of susceptibles amongst older children and adults compared to the prevaccination era. By the age of 10 years, 20% of the population are still seronegative, considerably more than the 8% observed in the prevaccination era [19]. Vaccination has thus resulted in a shift in the mean age of infection – with 13–18% of measles cases over 10 years of age during the 1970s compared to 40–50% in recent years [20]. A later age of infection is associated with more severe complications [21].

Routinely collected data from the United Kingdom show that those who receive a first dose are more likely to receive a second compared to those who are unvaccinated. If this pattern is repeated elsewhere in Europe, the initial priority in measles control is to achieve high first dose coverage. Once control is achieved, a second dose and/or catch-up can be introduced to immunize primary vaccine failures and those who have failed to receive their first dose (22, 23).

The proportion of low antibody positives for all countries was highest in the vaccinated age groups and lowest in the age groups > 30 years and partly in the age-groups of recently vaccinated children (1–3 or 4-years-old). This difference is probably explained by lower antibody titre after vaccination (or more rapid antibody loss) than after natural infection [24]. A cohort study in Finland demonstrated that vaccine

induced measles antibodies declined more rapidly in the absence of natural boosting than expected [25]. It will be important to both monitor the level and quality of vaccine-induced antibodies in the population and continue epidemiological surveillance in a period of decreasing opportunity for natural boosting. Furthermore, with vaccinated mothers living in a time of decreased opportunity for natural boosting, there is a need to monitor the persistence of maternal antibodies in infants, as this may influence the age of first vaccination. Variability observed in the proportion of seropositive infants in ESEN is partially a reflection of inter-country differences in the age (in months) of sampling, information that was not routinely collected as part of the project, thus limiting any interpretations.

The study also enabled an observation of the effect of the second dose of MMR on population immunity levels in some countries. The effect could not be studied in United Kingdom due to the narrow time frame between data collection and the introduction of the second dose and in Italy no second dose is given. However, in Finland and The Netherlands, no significant reduction was observed in the proportion seronegative in those cohorts eligible for a second dose compared to those receiving one. This observation could be due to the very high first dose coverage. However, a 12-year follow-up study conducted in Finland, found that after a brief increase in IgG antibody titre after the second dose, population antibody levels declined to pre-booster dose levels [26], suggesting that population serosurveillance may be limited in monitoring the impact of a second dose of MMR.

We can conclude that low susceptibility countries have achieved or are very close to measles elimination. Their continuing priority is to monitor coverage, strengthen disease surveillance with laboratory confirmation of suspect cases and to maintain high vaccine coverage in all geopolitical units for both vaccine doses. In moderate susceptibility countries, success in measles control is being achieved, but there is still endemic transmission and/or the risk of outbreaks as pools of susceptibles accumulate. Vaccine coverage assessment and disease surveillance may need to be strengthened (or introduced) and catch up campaigns may be needed to fill population susceptibility gaps. In the high susceptibility country – the priority is to increase infant vaccine coverage and reduce regional variation in coverage levels. Introduction of a second dose is only recommended once a coverage of $>80\%$ is reached. Serosurveillance can provide an important tool to support the evaluation of country vaccination programmes. The utilization of this data in mathematical models allows a quantitative evaluation of alternatives to determine the most appropriate vaccination strategy. Using these tools, the WHO European regional target of eliminating measles from the region by the year 2007 can still be achieved.

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Appendix: *Measles antibody serological results by age class in seven ESEN countries*

1. Denmark (collected 1994–8)

Age	Negative	Low positive	Positive	Total
0	14	1	23	38
1	48	2	46	96
2	23		74	97
3	25	2	74	101
4	17	1	53	71
5	8	3	37	48
6	10	4	98	112
7	7	6	87	100
8	9	4	86	99
9	14	4	80	98
10	12	6	82	100
11	9	5	86	100
12	6	2	91	99
13	3	1	95	99
14	2	5	92	99
15	1		99	100
16	5	1	94	100
17		1	38	39
18	1		46	47
19		1	53	54
20–24	1	2	196	199
25–29	2		199	201
30–34	1		198	199
35–39			201	201
40–49		1	207	208
50–59		1	200	201
60+	1	1	198	200
Total	219	54	2833	3106

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2. England and Wales (collected 1996)

Age	Negative	Low positive	Positive	Total
0	0	0	0	0
1	12	2	20	34
2	11	6	57	74
3	14	4	62	80
4	8	8	66	82
5	6	12	57	75
6	5	9	57	71
7	4	12	54	70
8	13	16	60	89
9	6	20	55	81
10	2	20	69	91
11	1	6	56	63
12	2	9	58	69
13	5	12	56	73
14	6	6	77	89
15	5	9	66	80
16	2	14	66	82
17	2	16	69	87
18	7	10	83	100
19	7	11	82	100
20–24	15	22	146	183
25–29	9	17	153	179
30–34	11	4	167	182
35–39	2	6	172	180
40–49	4	7	170	181
50–59	3	2	181	186
60+	11	1	173	185
Total	173	261	2332	2766

3. Finland (collected 1997–8)

Age	Negative	Low positive	Positive	Total
0	74	4	4	82
1	59	0	60	119
2	2	1	77	80
3	3	1	71	75
4	2	1	80	83
5	1	2	86	89
6	2	1	72	75
7	4	1	67	72
8	1	1	63	65
9	2	2	92	96
10	2	9	74	85
11	1	4	94	99
12	1	2	55	58
13	0	1	59	60
14	2	6	56	64
15	2	9	76	87
16	3	7	88	98
17	2	6	93	101
18	2	1	99	102
19	3	4	98	105
20–24	3	11	183	197

3. Finland (collected 1997–8) *continued*

Age	Negative	Low positive	Positive	Total
25–29	4	1	194	199
30–34	2	0	199	201
35–39	2	1	199	202
40–49	2	0	200	202
50–59	0	1	199	200
60−	0	0	203	203
Total	181	77	2841	3099

4. France (collected 1998)

Age	Negative	Low positive	Positive	Total
0	34	1	9	44
1	27	2	36	65
2	11	2	48	61
3	5	0	61	66
4	4	6	57	67
5	8	5	55	68
6	5	5	49	59
7	6	6	42	54
8	7	8	40	55
9	3	5	50	58
10	3	6	49	58
11	5	7	44	56
12	3	4	41	48
13	2	4	49	55
14	3	5	49	57
15	7	2	57	66
16	4	4	57	65
17	1	0	74	75
18	3	1	76	80
19	1	4	73	78
20–24	3	7	185	195
25–29	3	6	186	195
30–34	3	3	189	195
35–39	0	3	185	188
40–49	0	2	231	233
50–59	0	1	223	224
60+	2	2	410	414
Total	153	101	2625	2879

5. Netherlands (collected 1995–6)

Age	Negative	Low positive	Positive	Total
0	388	94	141	623
1	113	2	135	250
2	5	2	181	188
3	12	5	211	228
4	6	7	143	156
5	3	9	94	106
6	5	12	107	124
7	5	11	86	102

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5. Netherlands (collected 1995–6) *Continued*

Age	Negative	Low positive	Positive	Total
8	8	13	109	130
9	5	10	82	97
10	2	16	97	115
11	4	10	98	112
12	4	19	102	125
13	5	31	91	127
14	7	15	80	102
15	6	20	82	108
16	3	14	79	96
17	7	10	85	102
18	6	15	61	82
19	9	15	43	67
20–24	20	40	280	340
25–29	2	7	368	377
30–34	7	4	423	434
35–39		5	497	502
40–49	2	20	927	949
50–59	2	11	982	995
60+	1	22	1643	1666
Total	637	439	7227	8303

6. Italy (collected 1996–7)

Age	Negative	Low positive	Positive	Total
0	48	3	37	88
1	72	2	25	99
2	34	3	71	108
3	35	2	75	112
4	32	2	85	119
5	40	7	64	111
6	26	8	73	107
7	28	6	73	107
8	20	6	84	110
9	21	0	85	106
10	18	4	86	108
11	15	1	86	102
12	20	0	90	110
13	14	2	83	99
14	14	0	87	101
15	14	1	90	105
16	16	1	85	102
17	13	1	90	104
18	13	3	98	114
19	8	0	92	100
20–24	14	3	234	251
25–29	9	0	188	197
30–34	8	1	179	188
35–39	5	1	193	199
40–49	1	1	203	205
50–59	2	0	209	211
60+	5	0	199	204
Total	545	58	2964	3567

7. Germany (collected 1996)

Age	Negative	Low positive	Positive	Total
0	133	17	103	253
1	163	1	45	209
2	56	2	117	175
3	48	3	136	187
4	24	3	165	192
5	22	1	192	215
6	18	5	194	217
7	19	7	189	215
8	17	18	177	212
9	20	14	160	194
10	9	11	162	182
11	19	5	145	169
12	25	11	143	179
13	11	10	138	159
14	13	8	132	153
15	16	9	147	172
16	9	10	147	166
17	6	4	127	137
18	6	1	120	127
19	4	6	112	122
20–24	11	8	247	266
25–29	4	0	211	215
30–34	1	0	206	207
35–39	2	0	192	194
40–49	2	0	213	215
50–59	2	0	193	195
60+	0	0	225	225
Total	660	154	4338	5152

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