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An analysis of the incidence of measles in Turkey since 1960

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Background/aim: The aims of this study were to evaluate measles incidence and the effect of elimination strategy interventions on the disease from 1960 to 2014 in Turkey. The administration of measles vaccine started in the rural regions in 1970; it was carried out as a campaign along with the National Vaccine Campaign in 1985, and it has been employed as combined measles, mumps, and rubella under the scope of the Measles Elimination Program (MEP) since 2006 in Turkey. While a dramatic decrease in the reporting of measles was observed between 2000 and 2010, the number of the cases has increased since 2011.

Materials and methods: The time series of measles incidence was evaluated for possible structural changes with regression models using dummy variables, autocorrelated with error terms.

Results: The incidence of measles showed a statistically significant decline between 1985 and 1988 ($P = 0.0072$) and between 2005 and 2011 ($P < 0.0001$). However, a statistically significant increase in incidence was noted after 2013 ($P = 0.0008$).

Conclusion: Over the last 54 years, the pattern of measles cases demonstrated a significant decline in incidence. However, the increase in incidence in 2013 should be carefully analyzed and interpreted in terms of the MEP.

Key words: Burden of measles, measles elimination, measles incidence, Turkey

1. Introduction

Measles is the third vaccine-preventable infectious disease that the World Health Organization (WHO) aims to eradicate after elimination (1–6). Due to its high morbidity and mortality, measles is 1 of the 6 diseases that were included in the 1974 Expanded Immunization Program (EIP). Following elimination of the disease in the western Pacific region in 2002, WHO now aims to eliminate measles by 2020 in 5 more regions and the discussion on possible measles eradication strategies has already begun (2,6,7–13). WHO and combined measles, mumps, and rubella (MMR) initiatives have amended the target elimination year from 2010 to 2015 because epidemics occurred between 2007 and 2013 in the European region where the elimination program was being implemented (14–16). In 2010, WHO's Strategic Advisory Group of Experts on Immunization conducted a comprehensive evidence review to establish the biological and technical feasibility of measles eradication and concluded that measles can and should be eradicated (17).

1.1. Measles in Turkey

As shown in Table 1, according to the Ministry of Health data, a total of 66,111 cases of measles were reported in Turkey in 1969 before vaccination when measles was a nationally notifiable disease (18). Administration of the measles vaccine was initiated in 1970, primarily in rural regions (19).

Measles cases in Turkey and the elimination strategy of the Ministry of Health (1960–2013) are presented in Figure 1. The chronological history of fighting measles in Turkey started with National EIP in 1981; EIP, as well as a National Vaccine Campaign (NVC), was established in 1985 (20). The Measles Vaccination Acceleration Campaign was implemented in 1996, and a second-dose measles vaccine was administered to first-grade children in 1998. The Measles Elimination Program (MEP) has been running since 2006 (21–23). The purpose of this program was to eliminate measles in Turkey, maintain a low level of infection, halt indigenous virus transmission in Turkey by 2010, hinder the measles colonization due to importation, and prevent deaths. After 2006, "the Measles and Rubella Elimination and Prevention of Congenital Rubella Syndrome Program" was initiated and the triple MMR vaccine started.

The aim of this study was to evaluate measles incidence and the effect of elimination strategy interventions on the measles disease in 1960–2014 in Turkey.

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Table 1. The number of measles cases and measles incidence between 1960 and 2014 in Turkey.

Years	Number of measles cases	Measles incidence*
1960	15,926	57.9
1961	16,604	58.82
1962	10,347	35.76
1963	18,517	62.45
1964	17,312	56.96
1965	52,617	168.92
1966	50614	158.49
1967	42,906	131.01
1968	38,266	113.93
1969	66,111	191.94
1970	46,761	132.39
1971	43,002	118.74
1972	23,601	63.56
1973	43,271	113.65
1974	12,836	32.88
1975	24,347	60.83
1976	21,740	53.13
1977	16,123	38.6
1978	12,517	29.35
1979	11,745	26.98
1980	8618	19.39
1981	26,547	58.29
1982	8778	18.8
1983	31,515	65.84
1984	30,666	62.49
1985	14,695	29.21
1986	2267	4.4
1987	2194	4.19
1988	9279	17.42
1989	19,273	35.56
1990	11,372	20.63
1991	22,521	40.18
1992	24,626	43.21
1993	34,285	59.2
1994	23,733	40.34
1995	13,544	22.67
1996	27,171	44.78
1997	22,795	37.02
1998	27,120	43.42
1999	16,329	25,77
2000	16,010	24.91
2001	30,509	46.84
2002	7810	11.83
2003	5600	8.37
2004	8744	12.91
2005	1119	1.63
2006	34	0.05
2007	3	0
2008	4	0.01
2009	4	0.01
2010	7	0.01
2011	111	0.15
2012	349	0.46
2013	7405	9,68
2014**	529	0,65

*Incidence is defined as the number of cases per 100,000 individuals.
**Cases were only diagnosed in the first 9 months.

2. Materials and methods

The incidence of measles was calculated according to the number of reported measles cases and compared with population census data for each respective year. To satisfy the assumptions of the present model, the natural logarithm of the series was determined (24,25). The Box–Cox transformation for time series variables was applied to determine the need for stabilizing variance and satisfying the normality assumption. After the application of Box–Cox, the natural logarithm of the series was taken (25).

To analyze the significance of special events that might affect measles incidence, the transformed series was regressed with the intercept and some indicator functions for certain time periods. Using the history of measles incidence the following dummy variables were chosen:

$$I_1 = \begin{cases} 1, \text{ if } 1964 < \text{Year} < 1974 \\ 0, \text{ otherwise} \end{cases}$$

$$I_2 = \begin{cases} 1, \text{ if } 1973 < \text{Year} < 1975 \\ 0, \text{ otherwise} \end{cases}$$

$$I_3 = \begin{cases} 1, \text{ if } 1981 < \text{Year} < 1985 \\ 0, \text{ otherwise} \end{cases}$$

$$I_4 = \begin{cases} 1, \text{ if } 2005 < \text{Year} < 2011 \\ 0, \text{ otherwise} \end{cases}$$

$$I_5 = \begin{cases} 1, \text{ if } 2013 \leq \text{Year} \leq 2014 \\ 0, \text{ otherwise} \end{cases}$$

$$I_6 = \begin{cases} 1, \text{ if } 1985 < \text{Year} < 1988 \\ 0, \text{ otherwise} \end{cases}$$

$$I_7 = \begin{cases} 1, \text{ if } 1995 < \text{Year} < 1999 \\ 0, \text{ otherwise} \end{cases}$$

$$I_8 = \begin{cases} 1, \text{ if } 2001 < \text{Year} < 2011 \\ 0, \text{ otherwise} \end{cases}$$

To take into account problems due to autocorrelated errors, regression with dummy variables and autoregressive error models—specifically AR (1)—was performed (Figure 2).

All model diagnostics were satisfied. Parameter estimates of the models are given in Table 2. Variables I1–I8 presented the dummy variables. The first-order autoregression estimate was determined for the autocorrelated error model. Because variables I1–I3, I7, and I8 were not statistically significant at 5%, these variables were eliminated and the model was refitted. The probabilities provided in the last column of the table indicate that all model parameters are statistically

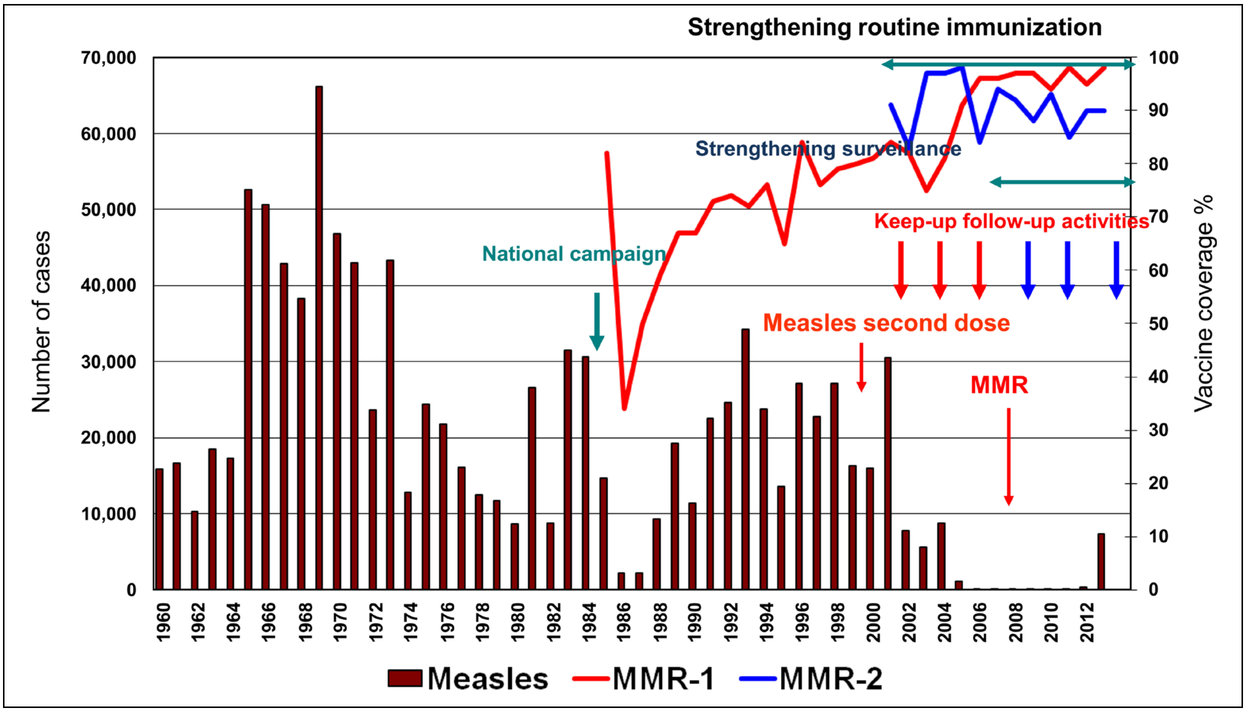

Figure 1. Measles cases in Turkey and elimination strategy (1960–2013).

Table 2. Parameter estimates of the regression with AR (1) error model.

Variable (years)	DF	Estimate	Standard error	*t* Value	Significance
I4 (2005–2011)	1	–3.1589	0.5917	–5.34	<0.0001
I5 (2013–2014)	1	2.9601	0.8265	3.58	0.0008
I6 (1985–1988)	1	–1.6567	0.5915	–2.80	0.0072
AR (1) Autoregressive model (1)	1	–0.9756	0.0261	–37.39	<0.0001

significant at 5% and should be included. Dummy variables I4–I5 decreased the incidence of measles, whereas I6 increased the incidence. Because logarithmic transformation was applied to the series before analysis, the exponent of the estimates was used to conclude the actual measles incidence. The coefficient of determination of the model was 95.49%, which indicated a very high variation in measles incidence and explained the variation in the given dummy variables.

SAS/ETS 9.2 (2008) software (SAS Institute Inc., NC, USA) was used to perform all statistical analyses. Figure 2 shows the close fit of the original and predicted values.

3. Results

When the 1960–2014 measles incidence in Turkey was analyzed using regression modeling, statistically significant drops were observed in 1985–1988 ($P \leq 0.0072$), i.e. after the 1985 NVC was implemented, and 2005–2011 ($P < 0.0001$), i.e. after the 2002 MEP and 2006 MMR vaccination were implemented (as seen in Table 2). The measles incidence decreased by 3.1589 units (incidence), on average, between 2005 and 2011 and between 1985 and 1988 with the presence of the fourth dummy variable; the presence of the fifth dummy variable resulted in a decrease of 1.6567 units (incidence), on average. However, in 2013 and during the first 9 months of 2014 (7405 and 529 cases), the log value of measles incidence increased to preelimination levels, i.e. 2.9601 units (incidence) on average ($P = 0.0008$).

4. Discussion

The aim of this study was to evaluate measles incidence since 1960 in Turkey. The Ministry of Health (MoH) in Turkey started measles vaccination in 1970 and the MEP

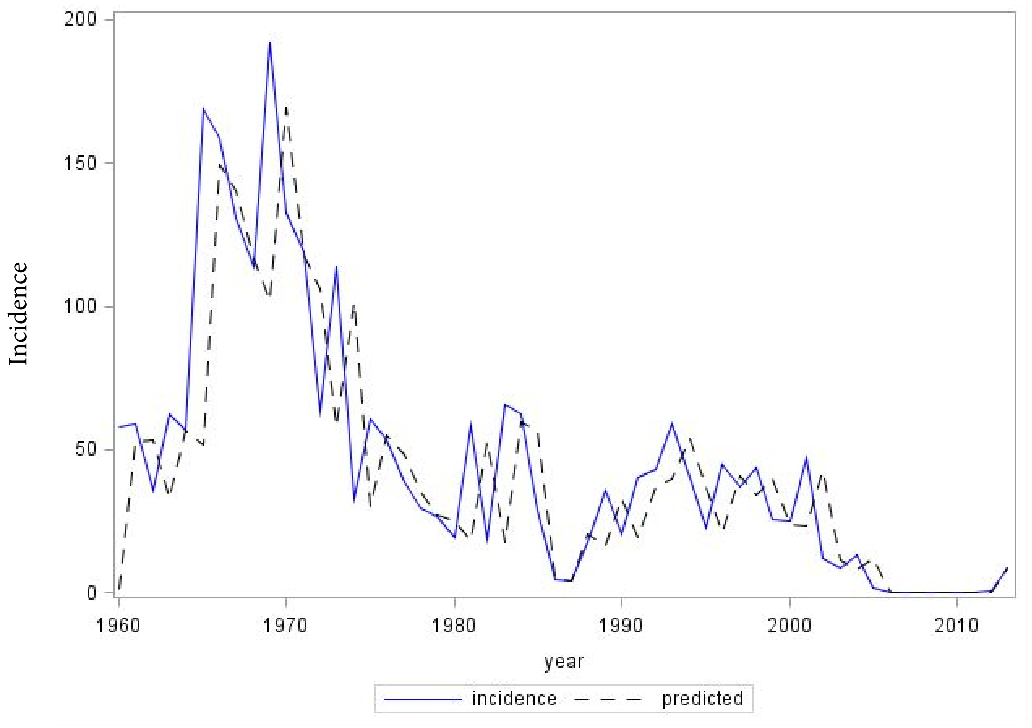

Figure 2. Time series plot of 54 years of measles incidence rates in Turkey and predicted values obtained using AR (1) regression error modeling.

in 2002. To show the significance of these interventions, a regression model was used. When the 1960–2014 measles incidence in Turkey was analyzed, 3 critical periods were detected (as shown in Figures 1 and 2).

A first drop period (1985–1988) followed the 1985 NVC. However, measles vaccination rates remained rather low prior to the 1981 EIP (25%–35%). A NVC was established in 1985, and 92% of the children <5 years of age were vaccinated at the end of this campaign (20). Following implementation of the NVC, the number of reported cases dropped from 2267 to 2194 in 2 years (1986–1987), as shown in Table 1.

A second drop period (2005–2011) followed the 2002 MEP and the onset of MMR vaccination program in 2006. The Measles Vaccination Acceleration Campaign was implemented in 1996, and a second-dose measles vaccine was administered to first-grade children in 1998. As shown in Table 1, in 2001, 30,509 measles cases were reported. The MEP has been running since 2002 (21–23). Accordingly, the 2003–2005 MEP implemented measles vaccination days, to administer catch-up vaccinations to individuals in sensitive cohorts (this initiative was separate from keep-up and follow-up activities). This program has been conducted as part of the Measles and Rubella Elimination and Prevention of Congenital Rubella Syndrome Program since 2006 and, accordingly, the MMR vaccine has been administered. All children attending elementary school were vaccinated during 2006–2008. Furthermore, a catch-up study was performed with individuals between 18 and 35 years of age in 33 provinces in 2009. The circular published by the MoH in 2010 reported the province-wide requirements for achieving measles surveillance, detecting potential epidemics, and effectively responding to and controlling epidemics in Turkey. In total, 18,216,897 children between 9 months and 14 years of age were vaccinated as part of the 2002 MEP, thereby achieving a vaccination rate of 96%. A dramatic drop in the number of measles cases was achieved, and no indigenous cases were reported in 2008–2010 (23). The decreased trend continued through 2012 with 349 cases (Table 1).

During the third period, the number of cases increased incrementally after 2013. As shown in Table 1, 7405 measles cases were reported in 2013. The MoH reported that this increase was not defined as an epidemic but instead described as a controlled increase in 2013, and all cases were classified as imported or related to an imported case (26,27,28). Unlike the MoH, in a report published by the Public Health Specialist Society in March 2013, the increase in measles was considered as an epidemic and, because of a large influx of refugees since 2013, this period was evaluated carefully (29). The official number of Syrian refugees in Turkey was 1,805,255, but the estimated number was around 2,500,000 (30). According to the report of "Disaster and Emergency Management Presidency" (DEMP), 28.2% of children aged less than 10 years in the camps and about 41.3% of children out of the camps were not vaccinated against measles. This posed a serious health threat for children among the local population (31). Moreover, the MoH reported that the importation risk increased because of Syrian refugees' low vaccination rates (28).

The WHO defines a measles epidemic according to the national vaccination program. A higher number of cases than expected can still be defined as an epidemic if the vaccination rates are low; however, in countries where elimination programs are implemented, an incidence that exceeds 1 case per 100,000 people is considered an epidemic (32). According to this criterion, the measles incidence of 2013 Turkey reflects an epidemic. Because of the high virulence and infection rate of the measles virus, epidemics can be observed in vaccinated and nonvaccinated groups in regions where elimination programs halt indigenous transmission (5,6,13,16,32–34).

The MoH reported that a significant portion of measles cases in 2013 included infants who had not yet been vaccinated. Therefore, the Measles Science Committee (MSC) recommended that first-dose MMR vaccination should be administered at 9 months instead of 12 months and second-dose vaccine should be administered at 12 months. The MSC also recommended that first-grade children should be vaccinated during nursery school, and military personnel, relatives of new patients, and disadvantaged and other low-socioeconomic groups should also be vaccinated by mobile health teams. Accordingly, approximately 4,000,000 people were vaccinated in 2013 (28,29). The increase in the number of cases was controlled using these precautions, and only 529 cases were detected by the end of September 2014. After the present analysis, the MoH announced that only 5 cases were added in the last 3 months in 2014. Statistical analysis was not repeated due to the small number of added measles cases. Considering the 2014 cases, it can be said that the MoH succeeded in these interventions in 2013 (28). The course of measles reveals that interventions could effectively reduce the incidence in Turkey. The 2013 increase in incidence needs to be carefully interpreted by program administrators. The MoH reported that 2013 cases were imported cases and their precautions were effective. Since 2005, epidemics reported in the European region (35–39), and the last epidemic experienced in Turkey, showed that it is impossible to eradication measles now (11,13,29,34,40). Particular factors including high infectivity, virulence, pathogenicity, inadequate cold chain, unsafe administration, groups who refuse vaccination or cannot be reached, incomplete protective properties of the vaccine, waning immunity, gradual increase in the sensitive pool over subsequent years, immigration, international travel, and so forth were the biggest barriers to eradication (11,13,29,34,40).

Over the last 54 years, the pattern in measles cases demonstrated that the incidence could be lowered effectively. However, the increase in incidence during 2013 should be carefully analyzed and interpreted in terms of the MEP. For diseases such as measles with high infection rates, it is important to reach 95% and more immunity in the populations. Therefore, the immunity levels of refugee children should be monitored carefully. Only the kindergarten children who were enrolled in the Ministry of National Education Schools were vaccinated during the 2013 outbreak. The effects of the Health Transformation Program (started in 2003), especially the primary care services, have to be considered. The performance of the contracting scheme (the immunization coverage rate of registered children) might affect the access of unregistered children to preventive services. Social awareness related to measles epidemic was relatively low in Turkey. Awareness among the community, motivation of health professionals for better coverage of preventive services, and motivation of people for utilization of preventive services are some necessary steps for the management of cases.

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