



# Which Type of Univariate Forecasting Methods Is Appropriate for Prediction of Tuberculosis Cases in Razavi Khorasan Province? A Need for Surveillance and Biosurveillance Systems

Nayereh Esmaeilzadeh<sup>1</sup>, Alireza Bahonar<sup>1\*</sup>, Abbas Rahimi Foroushani<sup>2</sup>, Mahshid Nasehi<sup>3</sup> and Mohammad Taghi Shakeri<sup>4</sup>

<sup>1</sup>Department of Food Hygiene and Quality Control, Faculty of Veterinary Medicine, Tehran University, Tehran, Iran

<sup>2</sup>Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup>Department of Epidemiology, Faculty of Health, Iran University of Medical Sciences, Tehran, Iran

<sup>4</sup>Department of Epidemiology and Biostatistics, Faculty of Public Health, Mashhad University of Medical Sciences, Mashhad, Iran

\*Corresponding author: Department of Food Hygiene and Quality Control, Faculty of Veterinary Medicine, Tehran University, Tehran, Iran. Tel: +98-9121305701, Email: abahonar@ut.ac.ir

Received 2019 July 10; Revised 2019 September 23; Accepted 2019 September 24.

## Abstract

**Background:** TB surveillance and preventing the further spread of the disease need the full knowledge of the biological characteristics influencing TB and detecting mathematical patterns to interpret the mechanism of TB spread. These models can provide explanations and knowledge of the dynamics of diseases and can be used for forecasting the ensuing values. To determine the possible number of patients, the time ahead is vital for decision making in public health. However, it is essential to determine forecasts' accuracy utilizing genuine forecasts. Thus, we obtained the TB cases from April 2007 until March 2018 in Razavi Khorasan province to develop a fit model and forecast the number of TB cases for the next 24 months.

**Methods:** We considered a time series of monthly incidence counts of TB in Razavi Khorasan province from April 2007 until March 2018. The data included total TB, pulmonary TB, new pulmonary TB, retreatment TB, and extrapulmonary TB cases. For choosing models and forecasting, we use about 20% of all data (24 data) for testing and the rest for training the model. The optimization of parameters was done automatically according to the smallest root mean squared error for these time-series analysis techniques with STATA. The models were EWMA models (single exponential and double exponential smoothers) and totally, we compared the quality of forecasts provided by EWMA models through the stand-alone measurement (RMSE).

**Results:** The patterns of raw series of total TB, pulmonary TB, and new pulmonary TB were almost the same. They illustrated slowly downward trends with oscillation around the trend that was a property of cyclic trend. For retreatment TB and extrapulmonary TB cases, reductions occurred over time although with no pattern. The results of statistical models indicated that the values of smoothing constants of all series were near zero that indicated a very smooth series with slowly changing counts. Total TB, pulmonary TB, and new pulmonary TB series had double exponential patterns with noisy and long-standing trend and they might be increasing in the 24 months ahead. Retreatment TB and extrapulmonary TB series had simple exponential patterns with noisy and without secular trends; they might be with no changes in the 24 months ahead.

**Conclusions:** The end TB strategy, MDG 6, target 8 is to stop and start to inverse the incidence of TB by 2015 and we joined this strategy in January 2006. However, TB control remains one of the main public health concerns. In recent years, our country has experienced immigrants from neighboring countries, sanctions or/and attacks with category C of biological agents in moving toward tuberculosis elimination. Our implementation requires changes in strategies and activities that should evolve over time. The findings of this study are helpful in achieving this goal.

**Keywords:** Tuberculosis, EWMA Models, Forecasting, Biosurveillance

## 1. Background

Tuberculosis (TB) is a necrotizing chronic or acute disease that usually involves the lungs although it can involve different body organs and tissues such as lymph nodes, pleura, pericardium, kidney, and bones. TB can occur as a

result of either a new infection with *Mycobacterium tuberculosis* or reactivation of a latent TB infection. Most cases in endemic countries, such as Iran, occur due to a new infection (1).

One of the Millennium development goals is to end TB

by decreasing the TB mortality rate by 50% compared to 1990, stopping or decreasing the TB incidence and prevalence until 2015, and decreasing the TB incidence to less than one case per million population by 2050 (2). The universal health coverage (UHC) has a vital role in this regard (2).

Generally, the disease burden of TB is decreasing but not at a speed sufficient to achieve the first milestones of the end TB strategy by 2020. The TB incidence rate should be decreased by 4% - 5% per year while it is decreasing by 2% per year (2). TB is reappearing in many countries as a public health crisis although it is not an emerging disease, it is an important reemerging disease. Reemerging TB might be caused by multidrug-resistant *M. tuberculosis* (category C of biological agents), the emergence of the HIV epidemics and a large number of immigrants from countries with common TB (3, 4).

During two decades, the TB incidence rate in Iran declined from 36 per 100000 in 1990 to 17 per 100000 in 2010, but it is not enough to reach the STB goal; hence, TB control is a prime concern for public health among policymakers. One of the important causes of this situation is the common frontier with three countries in which TB is a public health problem, i.e., Pakistan, Iraq, and Afghanistan (5, 6).

A way for the development of control programs and allocation of resources is reviewing temporal changes and forecasting. This method can have a major role in identifying health problems in the future (7).

## 2. Objectives

The aim of this investigation was to compare single exponential and double exponential smoothers to determine which model is more accurate for forecasting TB cases in Razavi Khorasan province and utilize this approach for surveillance and biosurveillance systems.

## 3. Methods

### 3.1. Study Setting

Razavi Khorasan province is located in the northeastern part of Iran in the vicinity of Afghanistan. It is the fifth-largest province in Iran, with an area of 118854 km<sup>2</sup>. Its population is about 6.5 million people, which makes it the second-largest populated province in Iran. The growth rate is 1.4%, which is higher than the national growth rate, with an incidence TB rate of about 14 per 100000 that is also higher than the national rate (about 11 per 100000).

### 3.2. Data Collection

We obtained the data from the Bureau of Tuberculosis the Center for Disease Control, the Ministry of Health and Medical Education of Iran.

The following definitions were used according to the national guideline of TB control:

A "new case" is a patient who has never received treatment for TB or who has taken anti-TB drugs for less than four weeks.

A "retreatment case" is a patient who has taken anti-TB drugs for at least four weeks.

Pulmonary tuberculosis is a patient who has Smear positive TB or Smear negative TB and extra pulmonary TB is as an infection of other parts of the body, except for lungs (1).

We presented a time series of monthly incidence counts of TB cases in Razavi Khorasan province between April 2007 and March 2018.

### 3.3. Model Fitting

For finding the best fitting model, according to previous studies (8, 9), we used two univariate time-series smoothing techniques (10, 11), including Simple Exponential and Double Exponential smoothing. We pooled the number of TB cases per month of daily cases; thus, 132 time-points (months) were obtained.

#### 3.3.1. Simple Exponential (SE) Smoothing

This method is applied for forecasting a time series when there is no trend or seasonal pattern, but the mean-time series gradually varies with time. The model needs one parameter ( $\alpha$ ) to create the fitted and forecasted values. The SE method is frequently applied to forecast the value of the time ahead, given the present and previous values.

$$S_t = \alpha x_t + (1 - \alpha) S_{t-1}$$

In this equation,  $S_t$  is the forecasted number of TB cases,  $x_t$  denotes the actual value in the period of the previous year, and  $S_{t-1}$  is the prior forecast.

#### 3.3.2. Holt's Trend (HT) Corrected Exponential Smoothing

It is also called the Double-Exponential method that is obtained by smoothing the smoothed series, as follows:

A. The exponentially smoothed series value

$$S_t = \alpha x_t + (1 - \alpha) S_{t-1}$$

in which,  $x_t$  is the raw series and  $\alpha_t$  and  $S_t$  denote the smoothing parameter and forecasted  $x_t$ , respectively.

B. The Double-Exponential smoother

$$S_t^{[2]} = \alpha S_t + (1 - \alpha) S_{t-1}^{[2]}$$

C. The difference exponentially smoothed series value trend estimate. The constant term:

$$a_T = 2S_T - S_T^{[2]}$$

D. The linear term:

$$b_T = \frac{\alpha}{1 - \alpha} (S_T - S_T^2)$$

E. The  $\tau$ , the-step-ahead out-of-sample prediction is given as follows:

$$\bar{x}_t = a_t + \tau b_T$$

To do the above-mentioned procedure, we used STATA V. 14.0 and Excel. The filters, which can produce forecasts, was run through the `tssmooth` command. Each of the two methods operates differently and is suitable for a specified type of forecasting task.

To compare the forecasts provided by these methods, we constructed several forecasted counts of TB, pulmonary TB, extrapulmonary TB, new TB, and retreatment TB.

For choosing models, we used about 20% of all data (24 data) for testing the model and 80% of the data for training the model. We used the testing data to measure how well the model forecasts the latest data (12).

The optimization of parameters was done automatically with STATA according to the smallest root mean squared error for these time-series analysis techniques. Smoothing constant ( $\alpha$ ) lies between 0 and 1 and controls the amount of inertia in the local mean. The values of  $\alpha$  near 0 produce very smooth series with slowly changing mean, and the values near 1 produce more volatile series with rapidly changing means (10). Forecast accuracy was calculated for 24 month-ahead forecasts by one of stand-alone measurement (RMSE) (12).

#### 4. Results

During 132 months from April 2007 to March 2018, there were 12406 TB cases in Razavi Khorasan province, including 9273 (74.7%) cases of pulmonary TB and 3133 (25.3%) cases of extrapulmonary TB. All of the extrapulmonary TB cases were new cases but 8797 cases of pulmonary TB were new TB cases and 476 cases were retreatment TB cases. The annual data are given in Table 1.

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Figure 1 represents the sketched time series plot of raw monthly counts of TB (type and site of the body) during the 11-year period from April 2007 to March 2018. According to raw series, the patterns of total cases of TB, total pulmonary TB, and new cases of pulmonary TB were almost the same. They illustrated a slow downward trend with oscillation around the trend that is a property of cyclic trend. For retreatment pulmonary TB cases and extrapulmonary TB cases, reductions occurred over time but with no patterns.

In the next stage to isolate the systematic component, we used two smoother techniques to remove noise components in a series. By using STATA on training data (April 2007 to March 2016), we obtained the optimization of parameters for five smoother techniques automatically. Table 2 gives the optimization of parameters for simple exponential and double exponential methods for total TB, pulmonary TB, new pulmonary TB, retreatment TB, and extrapulmonary TB series. The patterns are noisy with or without a secular trend. The values of smoothing constants of all series are near zero that indicates very smooth series with slowly changing counts.

For using genuine forecasts, we needed to examine the accuracy. We calculated the forecast accuracy measures for the two models for each series. Table 3 shows forecast accuracy measures for two smoother techniques for estimating based on testing data of each series and Table 4 indicates the actual and forecast values according to fitted models for the period from March 2016 to March 2018. Thus, total TB, pulmonary TB, and new cases of pulmonary TB series had double exponential patterns with noisy and secular trend and they might be increasing in the 24 months ahead. The two other series, retreatment TB and extrapulmonary TB series, had simple exponential patterns with noisy and without secular trend and they might be with no change in the 24 months ahead.

Figure 2 shows the sketched time-series plot of actual, fitted, and forecasted values for monthly models estimated based on the training data (April 2007 to March 2016) and forecasts for the next 24 months (March 2016 to March 2018) were produced according to the fitted model for each series.

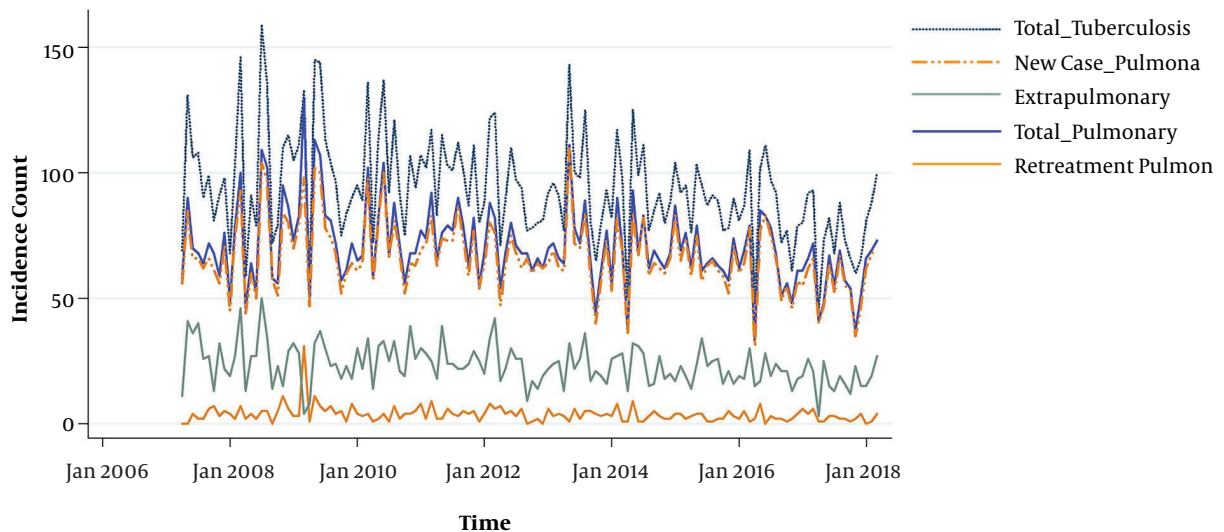
#### 5. Discussion

Adem and Ummu Atiqah (2009) showed that double exponential smoothing was the best forecasting model (9) and the results of the application of univariate forecasting models for TB cases in Kelantan (updated in 2014) indicated that the smallest MSE was related to Holt's exponential smoothing method (8). Therefore, we used EWMA

**Table 1.** Annual Data of TB Cases Reported in Razavi Khorasan Province<sup>a</sup>

Year	Total TB Cases	Pulmonary TB	New pulmonary TB	Retreatment Pulmonary TB	Extrapulmonary TB
March 2008	1192	852	803	49	340
March 2009	1258	926	876	50	332
March 2010	1229	928	868	60	301
March 2011	1230	906	857	49	324
March 2012	1227	904	854	50	323
March 2013	1057	806	761	45	251
March 2014	1159	871	831	40	288
March 2015	1098	839	802	37	259
March 2016	1063	797	764	33	266
March 2017	1004	757	722	35	247
March 2018	889	687	659	28	202

<sup>a</sup>Source: Bureau of Tuberculosis, Center for Disease Control, Ministry of Health and Medical Education of Iran.

**Figure 1.** Time series plot for TB cases in Razavi Khorasan province from April 2007 to March 2018**Table 2.** The Parameters of TB Series Data for Two Smoothers Techniques

Smoother Technique	Parameter	Total TB	Pulmonary TB	New pulmonary TB	Retreatment Pulmonary TB	Extrapulmonary TB
Simple exponential	$\alpha$	0.0351	0.0304	0.0213	0.0353	0.0306
Double exponential	$\alpha$	0.0266	0.0319	0.0313	0.0247	0.0001

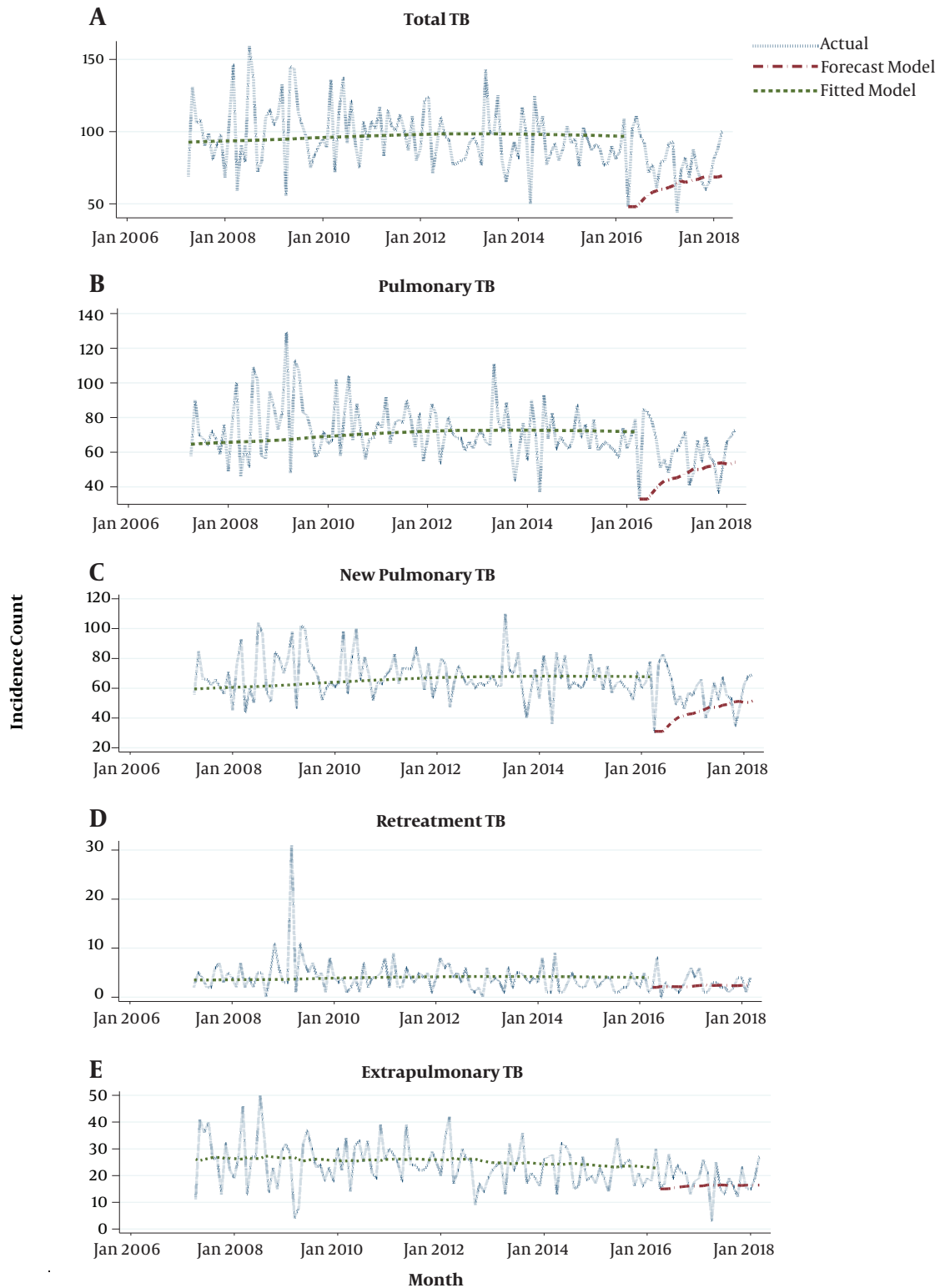
models to determine which forecasting models forecast TB cases more accurately in Razavi Khorasan.

We considered a time series of monthly incidence of TB in Razavi Khorasan province from April 2007 to March 2018. The data included total TB, pulmonary TB, new pulmonary TB, retreatment TB, and extrapulmonary TB cases. The models were EWMA models and the forecast accuracy

measure was RMSE (10-12).

According to RMSE, total TB, pulmonary TB, and new pulmonary TB series had double exponential patterns and retreatment TB and extrapulmonary TB series showed simple exponential patterns.

This study indicated that total TB, pulmonary TB, and new pulmonary TB, and retreatment TB cases had slowly



**Figure 2.** Actual, fitted, and forecasted values for monthly models according to the best fitting model for each series

**Table 3.** Forecast Accuracy Measures for two Smoother Techniques for Estimating Based on Testing Data of Each Series

Smoother Techniques	Total TB	Pulmonary TB	New pulmonary TB	Retreatment TB	Extrapulmonary TB
	RMSE	RMSE	RMSE	RMSE	RMSE
Simple exponential	27.58	24.33	24.85	1.98	6.18
Double exponential	26.19	21.67	20.95	2.01	6.53

**Table 4.** The Actual and Forecast Values According to Fitted Models for the Period from March 2016 to March 2018

Month-Year	Total TB		Pulmonary TB		New pulmonary TB		Retreatment Pulmonary TB		Extrapulmonary TB	
	Actual	Forecast	Actual	Forecast	Actual	Forecast	Actual	Forecast	Actual	Forecast
Apr -16	48	48	33	33	31	31	2	0	15	15
May -16	102	48.0266	85	33.0319	77	31.0313	8	2.0247	17	15.0002
Jun -16	111	48.0266	83	33.0319	83	31.0313	0	2.0247	28	15.0003
Jul -16	97	50.824	78	36.24536	75	33.82218	3	2.31869	19	15.0008
Aug -16	92	53.97702	68	39.18312	66	36.84744	2	2.206855	24	15.0035
Sep -16	72	56.27964	51	41.67207	49	39.24616	2	2.248315	21	15.0044
Oct -16	77	58.23121	56	43.42379	55	40.98609	1	2.240032	21	15.0063
Nov -16	61	59.06817	48	44.04002	46	41.61193	2	2.232021	13	15.0076
Dec -16	79	60.12939	61	44.93366	57	42.5705	4	2.176079	18	15.00889
Jan -17	80	60.31799	61	45.28812	55	42.93617	6	2.17036	19	15.00859
Feb -17	92	61.42967	66	46.42648	62	43.94972	4	2.26122	26	15.00929
Mar -17	93	62.54724	72	47.50823	66	44.79229	6	2.445113	21	15.01019
Apr -17	44	64.24016	41	48.84481	40	46.01767	1	2.525828	3	15.01248
May -17	73	65.91568	48	50.48575	47	47.42592	1	2.699909	25	15.01378
Jun -17	82	64.98405	67	50.12989	64	47.18816	3	2.626551	15	15.01148
Jul -17	68	65.5888	55	50.21968	52	47.38275	3	2.555794	13	15.01358
Aug -17	88	66.63331	69	51.47576	67	48.5964	2	2.583946	19	15.01367
Sep -17	73	66.90862	57	51.92725	55	49.02234	2	2.610992	16	15.01337
Oct -17	66	68.20635	54	53.21871	53	50.33505	1	2.588777	12	15.01427
Nov -17	60	68.67292	37	53.70361	35	50.85518	2	2.567302	23	15.01457
Dec -17	66	68.75546	51	53.97606	47	51.226	4	2.498348	15	15.01406
Jan -18	81	68.52091	66	53.18092	62	50.48365	4	2.480054	15	15.01576
Feb -18	88	68.60349	69	53.28442	68	50.49997	1	2.558765	19	15.01586
Mar -18	100	69.45696	73	54.30609	69	51.42195	4	2.63453	27	15.01596

increasing trends with noisy patterns while pulmonary TB and extrapulmonary TB had somewhat unchanging trends with noisy patterns. These findings indicated that TB is an infection with low virulence and sputum smear-positive (SS+) patients are more important for the transmission of disease (13). We can also conclude that the number of persons getting infection over the time ahead depends on the number of infectious cases at present.

In our study, we considered all types of pulmonary. If we separated these patients into sputum smear-positive and sputum smear-negative patients, we would have clearer patterns. As shown in a study that forecasted the incidence of smear-positive TB in Iran, it had a seasonal pattern (14).

There are different factors affecting the incidence of TB in various areas, such as weather, epidemiological transition, drug resistance, HIV, migration, and poverty. These

factors might increase the incidence of TB (5, 6, 15).

Another goal of this study was to do forecasting. We found that the number of total TB, pulmonary TB, and new TB cases might increase in the 24 months ahead. We forecasted no change in retreatment TB and extrapulmonary TB cases in the 24 months ahead.

A weakness of the forecasting method is that the trend of forecasting is influenced by the end value of the past data. If the last data level is higher than the earlier data, the forecasting section will have a growing trend and vice versa (11, 12).

The findings of this study and other studies from Iran and other countries indicate that the number of TB cases might increase (7, 14). In recent decades, our country has experienced immigrants from neighboring countries, sanctions or/and attack with category C of biological agents. Despite the fact that TB as a biological agent is not a

present public health threat, it can be a growing hazard in the future. The predicted growth of TB might be alarming. The prediction of bioterrorist attacks is difficult but they can impose heavy demands on the public health care system (16, 17). Finally, according to the end TB strategy, MDG 6, target 8 is to stop and start to inverse the incidence of TB by 2015 and we joined the end TB strategy in January 2006. However, TB control remains one of the main public health concerns. Although the goals and functions of TB control programs are constant, for moving toward TB elimination, our implementation requires changes in strategies and activities and should evolve over time. Recently, healthcare delivery systems are changing, as there is a trend toward the increased privatization of health care for the delivery of services; these can also create opportunities. A way to develop controlling programs and allocation of resources is reviewing the temporal changes and forecasting.

### Acknowledgments

This paper is extracted from the Ph.D thesis of Nayereh Esmailzadeh (Code: 7507011/6/28), Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran. The authors wish to thank the staff working at the Tuberculosis Office of the Ministry of Health.

### Footnotes

**Authors' Contribution:** Nayereh Esmailzadeh developed the original idea and the protocol, abstracted and analyzed data, and wrote the manuscript. Alireza Bahonar developed the original idea and the protocol and conducted the critical revision of the manuscript for important intellectual content. Mahshid Nasehi developed the original idea and participated in the acquisition of data, administrative, technical, and material support. Abbas Rahimi Foroushani conducted analysis and interpretation of data and critical revision of the manuscript for important intellectual content. Mohamad Taghi Shakeri conducted analysis and interpretation of data and critical revision of the manuscript for important intellectual content.

**Conflict of Interests:** There is no conflict of interest.

**Funding/Support:** There is no funding/support.

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