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Historical research into tuberculosis control strategies and the implications of mortality trends in Taiwan

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SUMMARY

SETTING: Taiwan.

OBJECTIVE: To analyse mortality trends to determine whether government organisation structuring and activities of disease control programmes affect outcomes.

DESIGN: We conducted a Joinpoint regression analysis to identify changes in TB mortality trends from 1971 to 2008 in Taiwan. The annual percentage change (APC) was calculated for the time segments on either side of the Joinpoints. Mortality data were extracted from the cause-of-death registry database of the Taiwanese Department of Health.

RESULTS: Between 1971 and 1987, the TB mortality rate dropped from 51 per 100 000 population to 13.4/100 000; during the period 1987–2000, it dropped from 13.4 to 7/100 000, with a lower APC; and from 2000 to 2008, it fell more rapidly, from 7 to 2.2/100 000, than during the previous two stages. These turning points are associated with organisational structure changes from the Joinpoint regression analysis.

CONCLUSION: We found that organisational structure and availability of resources play an important role in TB control. We recommend that other countries consider these vital factors to enhance the effectiveness of their TB control programmes.

KEY WORDS: tuberculosis control; mortality; trend analysis; JP regression; Taiwan

HOW do government organisation structure and the activities of disease control programmes affect outcomes such as mortality? According to the World Health Organization (WHO), contagious diseases no longer represent a major threat of mortality in the world;[1] however, tuberculosis (TB) still accounts for the majority of deaths caused by an infectious agent. TB not only has a severe impact in Asia, it still poses a formidable challenge to public health worldwide.[2,3] TB causes 25% of all avoidable deaths in the economically productive age groups,[4,5] and the TB treatment regimen is laborious and time-consuming. However, according to most previous studies, TB deaths are preventable if health authorities implement rigorous policies and if patients adhere to their treatment protocols.

Reduction in mortality is possible through various interventions such as medical treatment, health education and utilisation of disease control tools. These tools are diagnostics, drugs and vaccines, which are not 'magic bullets'.[6] In the West, the decline in the TB mortality rate was primarily due to the elimination of poverty, improved nutrition and better medical care (such as the use of streptomycin), which reduced deaths in the United Kingdom by 51% from 1948 to 1971.[7] However, TB remains a leading cause of death in low-income countries. Without adequate treatment, case fatality rates are high, over 50% within 5 to 8 years. With the availability of effective treatment, TB case fatality rates can be reduced from 50% to $<5\%$ within 5 years.[8–10]

Previous research has focused on the effectiveness of treatment,[11,12] the evaluation of interventions and the measurement of the disease burden from a clinical viewpoint. Few studies have investigated the public health perspective in health policy decision making. Some Asian countries such as Taiwan have made tremendous progress in the prevention (e.g., bacille Calmette-Guérin, X-ray screening and a computerised reporting system) and treatment of TB in the past decades. However, TB control in Taiwan faces the same predicament as in other industrialised countries. Most officials were optimistic in the 1980s, predicting a positive outcome in TB control based on the declining trend of incidence and mortality. However, if the TB control programme is inattentive, we may face a resurgence of TB as seen in the United States in the 1980s.

Health authorities used a centralised approach in the early (pre-1988) stage of TB control in Taiwan, at which time the Bureau of TB Prevention was responsible for TB control. In 1989, the organisational

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structure of TB control was absorbed into the Bureau of Chronic Disease Prevention and Treatment (CDPT). The Taiwanese government saw TB as a chronic disease and not as a major infectious disease, unlike other industrialised countries. Following a government reorganisation in 1999, the Center for Disease Control (CDC) was established, replacing the CDPT as the organisation responsible for leading anti-tuberculosis efforts in Taiwan. Following the establishment of the CDC, clinical and public health became completely separate. The former anti-tuberculosis organisation was dismantled, and TB control became part of the Taiwan CDC, providing all Taiwanese citizens with access to TB treatment.[13] Despite this organisational change, the government budget for TB control remained steady until the launch of the national TB programme (NTP) by the CDC in 2001.

Mortality trends reflect efforts made to improve TB control, such as the creation of a seamless process of surveillance, treatment and case management, with strong political commitment to provide funding to enable this process. The purpose of the present study was to use Joinpoint regression to analyse mortality trends with respect to organisational changes. These findings will help policy makers re-examine relevant issues related to mortality rates from field experiments and re-identify some useful decisions that other countries can learn from. TB control lessons in Taiwan may provide valuable information, especially regarding policy implementation and organisational changes.

METHODS

TB mortality data were extracted from the cause-of-death registry database maintained by the Department of Health of Taiwan. Population data were obtained from the household population registration system provided by the Ministry of the Interior of Taiwan. By law, all reported cases of death require a diagnosis of the cause of death by a qualified physician responsible for filling out the death certificate; this information is then recorded in the cause-of-death registry, in accordance with international standards. These data were used to calculate sex- and age-specific TB mortality rates. Causes of death were classified according to the International Classification of Diseases eighth revision (ICD-8) for the period 1971–1980 and the ninth revision (ICD-9) for the period 1981–2008, including 010-018 for ICD-8 and 010-019 for ICD-9, respectively.

To allow for changes in the composition of the population, the analysis included calculating age-standardised mortality rates (ASMR) using direct standardisation based on the 2000 WHO world standard population. The ASMR is the sum of the product of mortality rate in the *i*th age stratum (0–4, 5–9, . . . , ⩾85 years) in a given year in Taiwan and the proportion of standard population in the same age stratum in the same year. Analyses were undertaken for all ages as well as for three specific age groups: <45, 45–64 and ⩾65 years. This study also analysed trends by sex to generate more information.

We conducted Joinpoint (JP) regression analyses to identify changes in TB mortality rates from 1971 to 2008 in Taiwan. The JP regression methods were originally developed to identify points of significant inflection in cancer incidence/mortality trends.[14,15] Statistically significant changes in trends can be detected and quantified. The best fitting points are chosen in the final model.[16] This information assists in explaining or engendering further research on the causes of the changes in trends. The analysis begins with a minimum number of inflections (join-points) and tests whether additional JPs are statistically significant and should be added to the model.[17] The annual percentage change (APC) is calculated for each of these trends by means of a generalised linear model. Significant changes include changes in direction or in the rate of increase or decrease.[18] The JP regression analyses were performed using Joinpoint Version 3.2 software obtained from the US National Cancer Institute.[15]

RESULTS

The present study focused only on the turning points and APC (Table 1), rather than on real mortality rates. Figure 1 shows three turning points in the overall ASMR of TB; these occurred in the periods 1971–1987, 1987–2000 and 2000–2008, with APCs of

Table 1 Turning points and APC of TB mortality rate from Joinpoint regression

Mortality	Turning point 1	Turning point 2	Turning point 3	APC 1	APC 2	APC 3
Overall	1971–1987	1987–2000	2000–2008	−7.89	−5.37	−12.93
Sex						
Male	1971–1986	1986–2000	2000–2008	−7.23	−5.29	−13.33
Female	1971–1986	1986–2001	2001–2008	−9.67	−5.85	−12.32
Age group, years						
⩾ 65	1971–2002		2002–2008	−5.26		−12.37
45–64	1971–1987	1987–2003	2003–2008	−10.64	−8.27	−16.49
<45	1971–1985	1985–1998	1998–2008	−14.18	−3.28	−11.25

APC = annual per cent change; TB = tuberculosis.

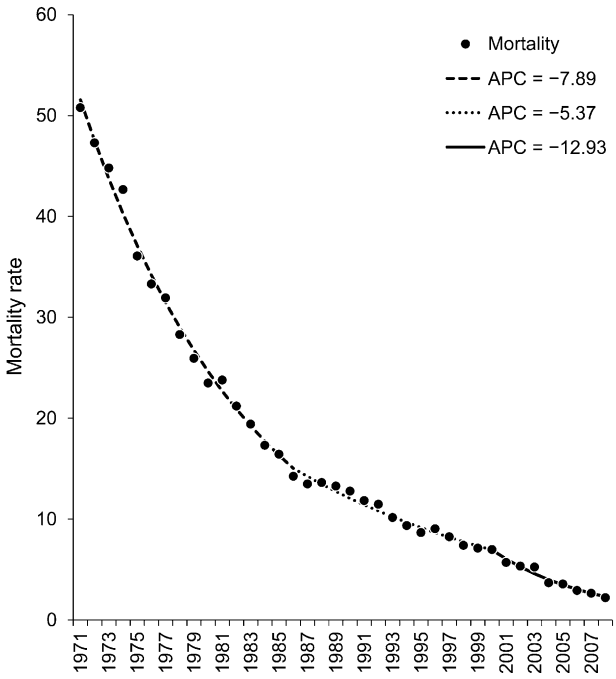

Figure 1 Mortality rate dynamics. APC = annual per cent change.

−7.89, −5.37 and −12.93, respectively. The APC characterises the trends of TB mortality rates in every slope. This means that rates were assumed to change at a constant percentage of the rate of the previous year. Between 1971 and 1987, the TB mortality rate dropped from 51 per 100 000 population to 13.4/100 000; during the following period (1987–2000), the mortality rate dropped from 13.4 to 7/100 000, with a lower APC. From 2000 to 2008, the mortality decreased more rapidly, from 7 to 2.2/100 000, compared to the two previous stages. Interestingly, the three turning points closely reflected the points of change in government structuring and organisational disease control measures, from the Bureau of TB Prevention in 1967 to the CDPT Bureau in 1988, then to the Taiwan CDC in 1999.

Table 1 illustrates additional data from the JP regression analyses by sex and age group. Females had a higher APC in the two previous stages despite being in the younger age group (<45 years). Furthermore, the mortality rate in the younger group declined more during the first turning point (1971–1985), but did not show the same performance compared to the other two age groups.

DISCUSSION

Our study found changes in organisational structure that were associated with changes in the rate of decline of TB mortality among the population. This study assumed that organisational change would have a greater impact on TB mortality trends because TB control requires an enhanced programme that comprehensively integrates resources. Effective control of any infectious disease usually demands an organisation with a high level of dedication to combining resources from public health and other medical entities.

Campbell used designs of field experiments to interpret different approaches to disease control.[19] Researchers used this method to determine whether programmes were effective and recognised outcomes that were based on immediate political implications. The mortality rate, for example, is an important index that is primarily used in the evaluation of TB control, as well as being basic and important information that identifies serious issues in public health.

In general, numerous factors affected trends in mortality rates. In the majority of situations, factors related to reduction in mortality rates were improved nutrition, urbanisation, vaccination, medical treatment and public health.[20] For example, in public health, extensive health education assisted patients in developing a better understanding of TB and adherence to treatment schedules.[21] Declining trends in mortality in Taiwan have supported the assumed effectiveness of the above improvements, particularly during the initial stages of TB control. Developing countries should commit more funds to basic resources such as public health infrastructure and nutrition to build a strong foundation for TB control.

The study also gives valuable insight into mortality rates by sex and age group. Lu et al. found that the mortality rate in Taiwan increased with age,[22] along with the turning points' yearly trend. Checking the age effect, the ⩾65 years age group has two turning points, while the other two age groups have three. This means that the mortality trend for those aged ⩾65 years changed only once. However, according to the moving APC trend, organisational change affected the 45–64-year age group more significantly than the other groups. The reason may be that TB prevention in the oldest group (⩾65 years) is more difficult due to comorbidies and other factors, whereas the youngest group (aged <45) received vaccines and medication.

Does medication then affect mortality trends more significantly than organisational change? TB chemotherapy positively affects population-based TB control efforts. In the past, more than 50% of TB patients died and 25% became chronically infectious due to a lack of effective medication and treatment.[23,24] In 1972, rifampicin (RMP) and isoniazid were being widely used in TB treatment, and Taiwan started providing treatment free of charge, using medications (including RMP) to treat TB, in 1978. In 1990, the standard 6-month treatment regimen was introduced. With adequate treatment, the mortality rate reached a turning point, with a decreasing trend. However, this study did not observe these turning points during or after the above-mentioned periods. We cannot deny that treatment was a major contribution, with

astonishing reductions in mortality rates in the first stage (1971–1987). However, TB control cannot rely solely on the use of medication; it also requires other public health efforts, which is the reason for the reversal of trends in the second stage.

Several other important TB control policies in Taiwan may be associated with the TB mortality rate (Table 2). For example, BCG vaccination was implemented in 1951. From 1984, the authorities computerised the TB patient registry and case management, and National Health Insurance (NHI), launched in 1995, enhanced the completeness of TB reporting. Two years later, the no-notification-no-reimbursement policy for unreported cases of active TB was introduced.[25] The Taiwan government also adopted a harm reduction programme for HIV and TB comorbidity that produced positive results.[26] However, these policies contributed little to the reduction in TB mortality rates. None of the aforementioned policies may have contributed more in changing the TB mortality rate than the organisational changes, as indicated in the Joinpoint regression.

Taiwan is a country of high population density and mobility, making case detection and management more difficult than if patients are treated in specialised TB clinics or hospitals. Some researchers worried over how organisational change from centralisation to decentralisation would affect TB control.[27] The results of this study showed that organisational changes correspond to turning points in TB mortality during the three stages illustrated in Figure 2, which displays the mortality rates during these three stages.

Another possible challenge encountered is lost educational value.[28] An inexperienced doctor who encounters an uncommon case of TB in an individual case history now has reduced ability to learn clinical skills and must rely primarily on publications.[29] Instinct and experience still play a major part in determining whether treatment should be administered.[30] Further, the government needed to integrate that system into a full-scale contact investigation network,[31–33] rapid laboratory results, an effective vaccine and screening policy, and an effective treatment strategy such as DOTS, without which TB control in such a brief period would have been extremely difficult.

Taiwan's experience shows that TB control requires not only effective medical treatment but also firm political commitment.[34,35] Historically, TB control operated independently in special programmes; in other words, the government combined personnel and budgets into an intensive operation. However, when the Bureau of TB Control ceased to exist, organisational change spread resources throughout the country, and the responsibility of TB control was transferred to the Chronic Disease Control Centers. The situation changed again after the Taiwan CDC was established, as CDC Taiwan received a larger budget for the TB control programmes. This study shows that organisational change had a greater effect on TB mortality trends, as TB control requires an enhanced programme that comprehensively integrates resources.

According to one study,[36] a single untreated TB patient can infect 10 to 15 persons. A successful TB programme needs political commitment.[37,38] Without intensive strategies for contact investigation, protection, prevention and treatment, success in the fight against TB will be far more difficult in the future.

We now face more challenges, such as multidrug-resistant TB (MDR-TB). The primary MDR-TB rate in Taiwan has increased from 0.2% in 1990 to the current 2.1%, a 10-fold increase in 10 years.[39] The public

Table 2 Major events related to TB control

Year	Events	JP turning point
1951	BCG vaccine introduced	
1955	Taiwan started to develop a comprehensive system of TB prevention, control and case management with support from the WHO	
1967	The government established the Taiwan provincial bureau of TB prevention and gave it the full responsibility for TB prevention and treatment. (TB Control Bureau, TB Control Yuan and TB Control Center)	
1972	RMP and INH used in treatment.	
1978	Introduction of treatment free of charge, using medications (RMP) to treat TB for the first 10 months	
1984	Computerisation of TB patient registry and case management	
1985	TB mortality lowered from the top 10 list	
1986	Drop below 10/100 000 (standard mortality rate)	
1988	The health authority optimistically predicted a lower TB mortality rate and devolved the power of TB control to the Bureau of Chronic Disease Prevention and Treatment (Chronic Disease Control Centers)	1987
1990	Most hospitals introduced the standard 6-month regimen for the TB patients	
1997	NHI discontinued drug reimbursement for unreported active TB	
2001	CDC Taiwan established: in charge of all infectious diseases	2000
	Roll-out of internet-based case reporting system, open access and strengthening of surveillance reporting	

TB = tuberculosis; JP = Joinpoint; BCG = bacille Calmette-Guérin; WHO = World Health Organization; RMP = rifampicin; INH = isoniazid; NHI = National Health Insurance; CDC = Centers for Disease Control.

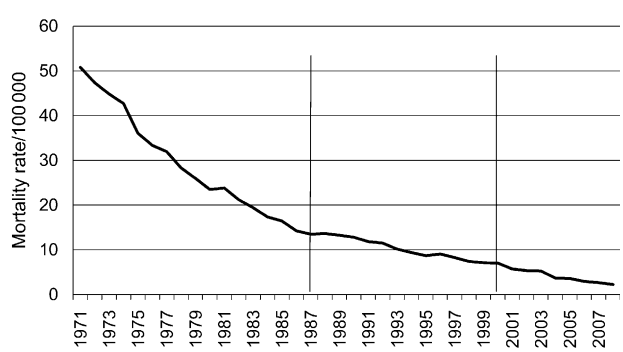

Figure 2 Trends in tuberculosis mortality during three stages of organisation.

should be informed that TB is not a stigma, but a treatable, preventable disease. The key to TB control lies in early detection and treatment and in combining public health resources and medical entities with the intensity of purpose that we have learned from our lessons.

CONCLUSIONS

This study found that organisational structure and the availability of resources play an important role in TB control. We recommend that other countries consider these vital factors to enhance the effectiveness of TB control programmes.

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RÉSUMÉ

CONTEXTE : Taiwan.
OBJECTIF : Analyser les tendances de mortalité indiquant dans quelle mesure la structuration des organisations gouvernementales et les activités d'un programme de lutte contre la maladie ont une influence sur les résultats.
SCHÉMA : Nous avons mené une analyse de régression Joinpoint (JP) pour identifier les modifications des tendances de mortalité par la tuberculose (TB) entre 1971 et 2008 à Taiwan. Le pourcentage annuel de modification (APC) a été calculé pour les périodes de temps de part et d'autre du JP. Les données de mortalité ont été prélevées dans la base de données du registre des causes de décès grâce au Département de la Santé de Taiwan.
RÉSULTATS : Entre 1971 et 1987, le taux de mortalité par TB a baissé de 51 à 13,4/100 000 ; pendant la période suivante (1987–2000) le taux de mortalité a baissé de 13,4 à 7/100 000 et l'APC a été plus faible. Entre 2000 et 2008, la mortalité a décru plus rapidement (de 7 à 2,2/100 000) par comparaison avec les deux étapes précédentes. Ces tournants dans la mortalité sont en association avec des modifications de la structure organisationnelle qui ressortent de l'analyse de régression Joinpoint.
CONCLUSION : Cette étude a démontré que la structure organisationnelle et la disponibilité de ressources jouent des rôles importants dans la lutte contre la TB. Nous recommandons que d'autres pays envisagent ces facteurs vitaux pour renforcer l'efficience de leurs programmes de lutte contre la TB.

RESUMEN

MARCO DE REFERENCIA: Taiwán.
OBJETIVO: Mediante el análisis de las tendencias de mortalidad por tuberculosis (TB), se buscó determinar si la organización gubernamental de la estructura y las actividades de un programa de control de la TB tiene repercusiones en los desenlaces clínicos de la enfermedad.
MÉTODOS: Se llevó a cabo un análisis de regresión lineal segmentada con el fin de detectar las modificaciones en las tendencias de la mortalidad entre 1971 y el 2008 en Taiwán. Se calculó el porcentaje anual de cambio (APC) en los intervalos de un lado y de otro de los puntos de inflexión. Los datos sobre la mortalidad se extrajeron de la base de datos del registro de las causas de defunción del departamento de salud de Taiwán.
RESULTADOS: La tasa de mortalidad por TB disminuyó de 51 por 100 000 habitantes a 13,4 por 100 000 entre 1971 y 1987; durante el período siguiente (del 1987 al 2000) esta tasa disminuyó hasta 7 por 100 000 habitantes, con un menor porcentaje anual de cambio. Entre el 2000 y el 2008, el ritmo de la disminución de la mortalidad fue todavía más acelerado (de 7 por 100 000 a 2,2 por 100 000) que en los dos períodos previos. El análisis de regresión lineal segmentada permitió establecer la relación entre estos puntos de inflexión y las modificaciones en la estructura de la organización del programa de control de la TB.
CONCLUSIÓN: El presente estudio puso en evidencia la importante función que cumple la estructura organizativa y la disponibilidad de recursos en la lucha contra la TB. Se recomienda que otros países tengan en cuenta estos factores primordiales, con miras a reforzar la eficacia de los programas de control de la enfermedad.