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**Original Article**

# Cost-Benefit Analysis of the Tsutsugamushi Disease Prevention Program in South Korea

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**SUMMARY**: The purpose of this research was to evaluate the economic value of the tsutsugamushi disease prevention program and to suggest whether to abolish or expand this program. A cost-benefit analysis was conducted to evaluate the economic feasibility of this prevention program. We collected cost data from 25 public health centers (PHCs) and the medical insurance data for all tsutsugamushi patients. We estimated the costs and benefits of the program using a macro-costing method. The estimated total cost was $1.22 million with a governmental cost of $697,000 and a cost of $521,000 to the PHCs. After the prevention program was implemented, $581 were salvaged from medical costs, $46 from non-medical costs, and $847 from productivity loss due to the reduced number of patients, with an estimated $6.66 million per year in total benefits of the program. The ratio of benefit to cost was found to be 5.5, making the economic value of the program significant. The net benefit should increase if the tsutsugamushi disease prevention program is continued and the implementation period is expanded to 10 years.

## INTRODUCTION

Tsutsugamushi disease is a zoonosis disease that is observed in the agricultural regions of Asia and on the Western Pacific islands (1–3). People in rural regions are often infected during outdoor activities in the fall, as the disease is transmitted to humans through trombiculid mites. Following transmission, infections consequently result in acute fever. Tsutsugamushi disease is categorized as a class 3 communicable disease and is regulated by the Korean government.

The incidence rate of tsutsugamushi disease is higher in Korea than in Japan (4). Over 6,000 cases of the disease are reported every year; the number of cases was 2,637 in 2001, 6,780 in 2005, 6,480 in 2006, and 6,022 in 2007. The number of patients is highest in the Jeonbuk, Chungbuk, Gyeongbuk, Gyongnam, and Chungnam provinces. The disease has spread rapidly with an average increase in the rate by 12.1% since 2001 (5). Although the number of reported cases increased from 2,637 in 2001 to 6,780 in 2005, the number of cases in 2007 was down from the reported cases in 2005, which is the year when the prevention program for tsutsugamushi disease was implemented.

Tsutsugamushi disease develops in vulnerable persons such as women and the elderly in rural areas. Women over 50 years of age are more often infected than other groups. Diagnosis of the disease is difficult because its patterns are similar to those of hemorrhagic fever with renal syndrome, leptospirosis, and eruptive fever, which occur during the same time of the year. Tsutsugamushi disease poses major health risks to residents in rural areas, as it is associated with severe complications such as acute renal failure and septic shock. Temporary cranial nerve palsy has also been reported as a complication of tsutsugamushi disease, and in some cases, if symptoms deteriorate, the disease can lead to myocarditis, meningitis, or local or systemic lymphadenopathy and splenomegaly. Because symptoms are not treated appropriately, 0–30% of patients with tsutsugamushi disease die of heart failure, dyscyclia, pneumonia, sepsis, and/or other complications (6).

Patients with tsutsugamushi disease experience severe medical complications. Thus, in most cases, costs associated with these complications, as well as the disease itself, are considerably high. Further, development of severe complications results in productivity loss during the treatment period. This has negative impacts not only on the household economy, but also on the agricultural economy. Therefore, the Korea Center for Disease Control and Prevention (KCDC) implemented a prevention program in 4 public health centers (PHCs) in 2004, which was later expanded to 25 PHCs throughout the country in 2008. The program aims to educate people about risk factors of tsutsugamushi disease, provide preventive materials, and improve the environmental conditions in vulnerable regions. Regarding educating people on the prevention of risk factors, PHCs distributed leaflets to the populations at risk and recruited staff to educate the farmers and to encourage farmers to take better preventive action such as cleaning up the remains of harvests in an attempt to decrease the density of rodents carrying trombiculidae. In addition to educating the public, PHCs also provided preventive materials such as arm warmers, work clothes, and repellents. The prevention program has reduced the increase in the total number of cases of tsutsugamushi disease since 2006 (5). The purpose of this paper was to evaluate

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the economic value of the tsutsugamushi disease prevention program by estimating the costs and benefits of the program and to suggest whether to abolish or expand this program.

## MATERIALS AND METHODS

As part of a cost-benefit analysis on the tsutsugamushi disease prevention program, we investigated the outcomes of the program with respect to their monetary value. In addition, the input costs for the program were comprehensively examined. This study calculated the benefits of the program by estimating the decrease in number of patients with tsutsugamushi disease after the implementation of the program by comparing the reported numbers with the expected numbers without the program. With the costs and benefits of the program being calculated from a social perspective, the net benefit and the benefit-cost ratio were estimated to assess the cost-effectiveness of the program. A sensitivity analysis was performed for the duration of the program.

**Prevention program of tsutsugamushi disease:** The prevention program was implemented in communities where tsutsugamushi disease occurs frequently. Twenty-six staff members were committed to the program, 3 from the KCDC, and 23 from 19 PHCs. Theses staff members provided arm warmers treated with a repellent agent and educated the people on measures to prevent the disease from spreading to other community members.

**Cost model for the tsutsugamushi disease prevention program:** The costs of the program included the costs of the PHCs for implementation, governmental costs, or indirect costs related to government subsidies provided to the PHCs, the administrative expenses of the in-charge department of the KCDC to support the program, as well as other costs. Administrative expenses were estimated by dividing the number of personnel working to support the program with the total number of personnel in the KCDC multiplied by the total budget of the KCDC. The costs of the PHCs included the budget for the prevention program, the administration, and labor expenses.

The types of costs for the prevention program are shown in equation 1, and the total cost refers to the sum of the governmental and PHC costs. A gross costing method was used. Governmental costs are presented in equation 2, whereas costs of the PHCs are presented in equation 3. Although the time cost of residents participating in the prevention program should be considered as other costs, it was excluded in this model because the data were not available.

$$C = GC + PHC \quad \text{(equation 1)}$$
$$GC = GS + AE + OE \quad \text{(equation 2)}$$
$$PHC = BDG + ALE \quad \text{(equation 3)}$$

GC, governmental costs; PHC, costs of the PHCs; GS, governmental subsidies for the tsutsugamushi disease prevention program; AE, KCDC administrative expenses (indirect cost); OE, other expenses (indirect cost); BDG, PHCs' budgets for the prevention program excluding the subsidy; ALE, administrative and labor expenses at the PHCs

**Benefit model for the tsutsugamushi disease prevention program:** The prevention program impeded the increase in the rate of incidence for tsutsugamushi disease, resulting in decreases in medical costs, non-medical costs, and productivity losses; these can be considered the benefits of the prevention program. The reduced number of patients after the prevention program was estimated by performing trend analysis using the existing tendency of incidences.

The benefits of the program were estimated to be the sum of the savings in medical costs, non-medical costs, and productivity losses and were measured using the macro-costing approach. The calculation of program benefits is shown in equation 4. The decline in the number of patients was considered to be the outcome of the prevention program and was calculated by the difference between the predicted and actual number of patients (equation 5). The incidences were predicted using trend analysis (equation 6).

$$TB = \Delta N \times (MC + NMC + PL) \quad \text{(equation 4)}$$
$$\Delta N = Nb - Na \quad \text{(equation 5)}$$
$$Nb = \beta_1 + \beta_2 T + \beta_3 T^2 \quad \text{(equation 6)}$$

$\Delta N$, decrease in the number of patients after the prevention program; MC, medical costs; NMC, non-medical costs; PL, productivity losses; Nb, predicted number of patients with tsutsugamushi disease without implementation of the program; Na, actual number of patients with tsutsugamushi disease after the implementation of the program; T, year-1993

The medical costs of the treatments for tsutsugamushi disease were divided into inpatient and outpatient costs according to the type of medical services (equation 7) and were estimated using the National Health Insurance database. Data for out-of-pocket payments came from the National Health Insurance Corporation's survey (7), and information on the prices of medical services, pharmaceuticals, and materials used in this study are based on the report of the Health Insurance Review and Assessment Service (8). Fatality-related costs were not included, as deaths caused by tsutsugamushi disease have not been reported. The medical costs of tsutsugamushi disease per day were obtained by analyzing the medical records of patients treated for the disease, and the ratio of inpatients to outpatients was determined using the KCDC report published in 2006 (9). Since most of the cases of tsutsugamushi disease were treated in hospitals, the treatment costs are relatively higher than the average costs (7).

$$MC = InMC + OutMC$$
$$InMC = \sum_{i=1}^{t} InPCi + InNHC$$
$$OutMC = \sum_{i=1}^{t} OutPCi + OutNHC \quad \text{(equation 7)}$$

InMC, inpatient's medical costs; OutMC, outpatient's medical costs; InPCi, inpatient's medical costs per day; OutPCi, outpatient's medical costs per day; InNHC, inpatient's out-of-pocket payments; OutNHC, outpatient's out-of-pocket payments; t, number of days for treatments

Non-medical costs of tsutsugamushi disease consisit of travel expenses for visiting medical institutions and other expenses (10).

As an indirect cost of tsutsugamushi disease, productivity losses caused by the disease were calculated by the number of lost working days (11) and the indirect and direct productivity losses per capita were estimated using the inter-industry table of the Bank of Korea (equation 8) (12). Between 2000 and 2005, before the prevention program was implemented, an average of 6.5 persons died per year and after the implementation, the number of deaths caused by the disease was reduced to 2.5–4.0 on average. However, the numbers were small and not stable. It is not clear whether the decrease in deaths was an effect of the prevention program. In addition, because the majority of individuals who received benefit from the program were elderly, this study excluded early death-associated income loss.

$$PL = FV \times PLD \quad \text{(equation 8)}$$

FV, value added in agriculture; PLD, number of lost working days caused by tsutsugamushi disease.

## RESULTS

**Costs:** The governmental and PHC costs for the program were estimated using the cost model shown in Table 1. The total cost for the program was $1.22 million, with governmental costs of $697,000 and PHC costs of $521,000.

**Benefits:** The tsutsugamushi disease prevention program was initiated in November 2004, and the number of PHCs running the program increased from 4 in 2006 to 25 in 2008. The program was not actively conducted in the first year of implementation in 2005, and expansion of the program did not begin until from 2006. After the implementation of the program, the increase in the rate of incidence was curbed. The effectiveness of the prevention program was estimated by a regression model (equation 6) using KCDC data from 1994 to 2005 before the program was implemented. We used 5 different models to estimate the trend of the number of patients with tsutsugamushi disease and compared the results for these 5 models; the obtained $R^2$ was 0.6714 in log, 0.8451 in linear, 0.8953 in power, 0.9135 in exponential, and 0.9469 in quadratic models. Finally, a quadratic model was used for estimation (equation 9). The figures in parentheses in the equation indicate ***P***-values.

$$\underset{(0.317)}{Nb = 648.78} - \underset{(0.017)}{314.54T} + \underset{(0.004)}{64.73T^2} \quad \text{(equation 9)}$$
$$R^2 = 0.9469,\ F = 60.968\ (0.000)$$

The number of patients with tsutsugamushi disease reported to the KCDC is 6.6% lesser than the number of patients reported in the health insurance database, so the estimated number of patients in equation 9 was adjusted according to the database. The final estimated number of projected cases that would have been reported without the implementation of the prevention program, after adjustment by 6.6%, was 11,243 in 2008, whereas the actual number of patients from the database was 6,724. Thus, the implementation of the program was estimated to have reduced the number of patients by 4,519.

The benefits in medical costs were estimated to be $581 from the decrease in the number of patients (Table 2), while $46 was saved from the non-medical costs and $847 from productivity losses. Therefore, the benefit per capita was $1,474, and the reduced number of patients was 4,519; thus, the total benefits of the program were estimated to be $6.66 million per year (Table 1).

**Net benefit and benefit-cost ratio:** With the estimated costs and benefits, the economic validity of the tsutsugamushi prevention program was assessed. The net benefit of the program was expected to be $5.45 million, 5.5 times greater than the estimated costs. This analysis shows that the benefits of continued operation of the program far outweigh the associated costs (Table 1).

**Sensitivity analysis:** To evaluate the economic feasibility of the tsutsugamushi disease prevention program in the future, a two-way sensitivity analysis was performed by considering to the number of patients prevented and the duration of the program. The costs and benefits were adjusted by the medical inflation rate for the last 3 years (2.4%), growth rate of the consumer price index (3%), and growth rate of farmers' incomes (1.03%).

Trend extrapolation was used to project the number

Table 1. Cost benefit analysis of tsutsugamushi disease prevention program

| | Type | Cost |
|---|---|---|
| Costs | Governmental costs | 697 |
| | Government's subsidy to PHCs | 95 |
| | KCDC administrative expenses | 573 |
| | KCDC other expenses | 29 |
| | PHC costs | 521 |
| | PHC budget for the prevention program | 371 |
| | Administrative and labor costs | 150 |
| | Total costs | 1,218 |
| Benefits | Benefits per capita | 1,474 |
| | Savings in medical cost | 581 |
| | Savings in non-medical cost | 46 |
| | Savings in productivity loss | 847 |
| | Patients prevented (persons) | 4,519 |
| | Total benefits | 6,663 |
| Net benefit | | 5,445 |
| Benefit-cost ratio | | 5.5 |

Unit of costs: Total benefit and net benefit is US 1,000 dollar. Unit of benefits per capital is US dollar.
KCDC, Korean Center for Disease Control; PHC, public health center.

Table 2. Per-capita total medical costs

| | Outpatient cost | Inpatient cost | Average cost[1] |
|---|---|---|---|
| Percentage of patients | 41.0 | 59.0 | 100.0 |
| Payments by NHI | 138 | 592 | 406 |
| Co-payments | 82 | 145 | 119 |
| Out-of-pocket payments | 40 | 67 | 56 |
| Total medical costs | 260 | 804 | 581 |

Cost unit is US dollar.
[1]: Average costs = outpatient costs × percentage of outpatient + inpatient costs × percentage of inpatient.
NHI, National Health Insurance.

Table 3. Number of patients decreased by the prevention program

| Year | No. of patients without prevention program[1] | | | No. of patients with prevention program[2] | No. of decreased patients | | |
|---|---|---|---|---|---|---|---|
| | Lower 95% | Mean | Upper 95% | | Lower 95% | Mean | Upper 95% |
| 2008 | 9,717 | 11,243 | 12,768 | 6,724 | 2,993 | 4,519 | 6,044 |
| 2009 | 11,530 | 13,055 | 14,581 | 6,494 | 5,036 | 6,562 | 8,087 |
| 2010 | 13,481 | 15,007 | 16,532 | 6,271 | 7,210 | 8,735 | 10,261 |
| 2011 | 15,571 | 17,097 | 18,622 | 6,056 | 9,515 | 11,040 | 12,566 |
| 2012 | 17,800 | 19,325 | 20,851 | 5,849 | 11,951 | 13,476 | 15,002 |
| 2013 | 20,167 | 21,693 | 23,218 | 5,648 | 14,519 | 16,044 | 17,570 |
| 2014 | 22,673 | 24,199 | 25,724 | 5,455 | 17,218 | 18,744 | 20,269 |
| 2015 | 25,318 | 26,843 | 28,369 | 5,268 | 20,050 | 21,575 | 23,101 |
| 2016 | 28,101 | 29,627 | 31,152 | 5,088 | 23,014 | 24,539 | 26,065 |
| 2017 | 31,023 | 32,549 | 34,074 | 4,913 | 26,110 | 27,636 | 29,161 |
| 2018 | 34,084 | 35,610 | 37,135 | 4,745 | 29,339 | 30,865 | 32,390 |

1): The number of patients expected without prevention program was estimated by a regression analysis using time trend variable. Lower and upper bounds of 95% confidence interval were suggested for the estimated number of patients.
2): The number of patients with prevention program was estimated by an average decreasing of 3.7% in 2006–2008.

Table 4. Two-way sensitivity analysis by patients prevented and program period

| | 2008 | 2011 | 2013 | 2018 |
|---|---|---|---|---|
| Costs | 1,218 | 1,331 | 1,543 | 2,074 |
| Benefits per capita | 1,474 | 1,553 | 1,795 | 2,833 |
| Patients prevented (persons) | | | | |
| upper 95% | 6,044 | 12,566 | 17,570 | 32,390 |
| mean | 4,519 | 11,040 | 16,044 | 30,865 |
| lower 95% | 2,993 | 9,515 | 14,519 | 29,339 |
| Benefits | | | | |
| upper 95% | 8,909 | 19,515 | 31,538 | 91,762 |
| mean | 6,661 | 17,133 | 28,807 | 87,403 |
| lower 95% | 4,412 | 14,776 | 26,061 | 83,118 |
| Net benefits | | | | |
| upper 95% | 8,909 | 18,297 | 30,207 | 90,219 |
| mean | 5,445 | 15,801 | 27,264 | 85,330 |
| lower 95% | 4,412 | 13,558 | 24,730 | 81,575 |
| Benefit/Cost ratio | | | | |
| upper 95% | 7.3 | 14.7 | 20.4 | 44.2 |
| mean | 5.5 | 12.9 | 18.7 | 42.1 |
| lower 95% | 3.6 | 11.1 | 16.9 | 40.1 |

Unit of costs: Total benefits and net benefit is US 1000 dollars. Unit of benefits per capital is US dollar.
1): Medical cost in future was adjusted by the medical inflation rate of 2.4% in last 3 years.
2): Non-medical cost in future was adjusted by a 3.0% growth rate of consumer price index.
3): Productivity loss in future was adjusted by a 1.03% growth rate of farmer's income.

of tsutsugamushi cases in the absence of the program for the year of 2011 (in 3 years), 2013 (in 5 years), and 2018 (in 10 years); 3 scenarios were included in these projections, the lower bound, mean, and upper bound of 95% confidence interval. These projections were estimated by applying the average rate of change in the number of reported cases from 2006 to 2008. Bases on these projections, the full operation of the prevention program is expected to reduce the number of patients in each year by 9,515 (lower 95%), 11,040 (mean), 12,566 (upper 95%) in 2011, 14,519 (lower 95%), 16,044 (mean), 17,570 (upper 95%) in 2013, and 29,339 (lower 95%), 30,865 (mean), 32,390 (upper 95%) in 2018 (Table 3). Therefore, if the prevention program is continuously implemented, the net benefit would be \$13.56–18.30 million in 2011, \$24.73–30.21 million in 2013, and \$81.58–90.22 million in 2018, and the benefit-cost ratio will increase from 11.1–14.7 in 2011 to 40.1–44.2 in 2018 (Table 4). In addition, we observed that the variation in net benefits and benefit-cost ratios due to uncertainty will decrease as the prevention program continues (Table 4).

## DISCUSSION

This study was performed to assess the economic feasibility of a program implemented by the government in 2004 to prevent tsutsugamushi disease; the incidence rate of this disease has increased continuously since the first recorded patient in 1951. Symptoms of tsutsugamushi disease are similar symptoms to those of other communicable diseases that also occur during the fall. Thus, clinical symptoms are not sufficient for definitive diagnosis, and serological examination or rickettsia culture is needed to distinguish tsutsugamushi disease from other diseases. Tsutsugamushi disease can lead to complications in the liver, kidneys, and lungs (13), and in 53.3% of the cases, this disease is associated with hematological changes such as anemia, leukocytosis, and thrombocytopenia (14). Because tsutsugamushi disease is difficult to diagnose at an early stage, proper treatment is often not provided, resulting in a higher occurrence of complications, which produce considerable social costs.

Tsutsugamushi disease is not transferred between humans, but is transmitted by the larvae of acarids, which increases in numbers in fall. Therefore, one of the most effective preventive measures is to prevent acarids from sticking to the skin while handling agricultural products. The prevention program, which expanded from 4 PHCs in 2005 to 25 PHCs in 2008, distributed arm warmers and repellents to farmers, as well as educated them on how to use these devices while working.

Since the implementation of this prevention program in 2005, the incidence rate of this disease has decreased. For examples, the number of patients with tsutsugamushi disease in Chyeongyang county, Chungcheong province, accounted for 73% of the total reported cases of communicable disease in 2006, but the rate dropped sharply to 43% in 2007. Because of the intensive implementation of the prevention program, the incidence rate of tsutsugamushi disease has been effectively mitigated.

The aim of the tsutsugamushi disease prevention program is to decrease the rate of infection by focusing on the residents of rural areas, who are most vulnerable to this disease and its associated complications. The program is operated by 25 PHCs in rural areas, with total costs of $1.22 million per year. In this study, total benefits and net benefits were estimated to be $6.66 million and $5.45 million, respectively, and the program was concluded to be sufficiently cost-effective, with a benefit to cost ratio of 5.5. These findings suggest that it would be worthwhile to increase the budget of the tsutsugamushi disease prevention program to allow for the expansion of the program into additional provinces. Moreover, as the range of tsutsugamushi disease has extended beyond the rural areas in the southern region to the urban areas in the central region due to the rising temperatures, the number of patients is likely to increase rapidly (15). Therefore, the benefit of the prevention program is expected to be greater than $6.64 million in future years. In addition, the benefits estimated in this study are likely to be underestimated because we based our estimates solely on reductions in actual expenditures. The monetary benefit of this prevention program calcurated using the willingness to pay (WTP) approach was reported to be as much as $62.74 million (10). Therefore, the net benefit was $40.95 million, and the benefit-cost ratio was 34.6 times the benefit-cost ratio estimate in this study. In our study, a two-way sensitivity analysis showed that although variations in net benefit and benefit-cost ratio resulting from a decrease in the number of patients could increase the uncertainty of the prevention program, the benefits would be maximized and the variations would reduced when the prevention program continuously operated. The net benefit and benefit-cost ratio are estimated to increase to $85.36 million and 42.1, respectively, on an average, in 10 years, so the continuous operation of the program is clearly required.

Compared with the benefit-cost ratios of prevention programs for pediatric meningitis, 0.27 (16); chickenpox, 1.83 (17); and measles, 1.03–1.27 (18,19), we found that the tsutsugamushi disease prevention program was more cost-effective. Among the other prevention programs mentioned, the tsutsugamushi disease prevention program had a relatively lower input cost. While the high costs of prevention programs for other communicable diseases can be largely attributed to the costs of vaccinations, the program for tsutsugamushi disease distributes repellents and arm warmers; therefore, the purchasing budget is trivial, as these items are much cheaper than vaccinations.

In this study, the costs for the program were divided into governmental and PHC costs, where the latter was considered to be the program costs of 25 PHCs in regions with high prevalence rates of tsutsugamushi disease. Although other PHCs aside from the aforementioned 25 also operate as part of the program, they were excluded from this study because their data were not available, and their programs were not significant in scope. Thus, the estimated input cost could be lower than the actual level.

This study has limitations in that the estimated benefits of the program may differ depending to the number of cases prevented and the duration of the program. Though the change in net benefit was predicted using sensitivity analysis, the optimal size of the program for generating the maximum benefits could not be estimated accurately. With a scaled up program, the increased rate of the total benefit is commonly reduced, and the total cost increases based on the law of diminishing returns. The conventional theory indicates that the net benefit of this prevention program increases at the initial stage, reaches a maximum, and thereafter declines as the scale of the program increases. The maximum net benefit is the point where the marginal benefit of the program is equal to the marginal cost. However, it is empirically difficult to determine the optimal size of the prevention program or the maximum net benefit point. The results of the sensitivity analysis show that the ratio of benefit to cost would significantly increase to a considerable level even after expanding the program beyond the current scale, implying that the expansion of the program would be rational. However, this result largely depends on the estimation model used for trend analysis. If the observed data for the number of future patients indicate a trend with a decreasing rate, the results will be different.

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**Conflict of interest** None to declare.

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