The Impact of Prevention and Control of Infectious Disease Law on Diarrhoea Control: A 5-year Evaluation in Multiple Provinces in Vietnam.

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Key Messages
• This study used a segmented intervention analysis which provides an appealing methodological framework to assess the impact of a health policy, the law of prevention and control of infectious disease (LPCID) in a developing country;
• The results of this study revealed the significant impact of the Law on Prevention and Control of Infectious Diseases in reducing 48% of diarrhoea incidence after 5 year of its implementation across Vietnam.
• These findings demonstrate the effectiveness of collective actions and regulations on infectious disease control in developing countries.
• Further studies should be conducted to better understanding the cost-effectiveness, acceptability and sustainability of each component of the LPCID in Vietnam.

Acknowledgment: DP was supported by the Post-doctoral Fellowship Award of Griffith University, Queensland, Australia.

Word count: 2,999

Key words: The law of infectious disease control, diarrhoea, impact evaluation, Vietnam
Abstract

**Introduction:** To address the burden of infectious diseases such as diarrhoea, the Vietnamese government has enacted the Law on Prevention and Control of Infectious Diseases (LPCID) since July 2008. However, no evaluation of the impact of the LPCID has been conducted. This study aims to evaluate the impact of the LPCID on diarrhoeal control for the 5 years following the implementation of LPCID in Vietnam.

**Methods:** We used an interrupted time series design using a segmented regression analysis to estimate the *province-level* impact of LPCID and then used random-effect meta-analysis to estimate the pooled effect sizes of the *country-level* impact of LPCID on diarrhoeal control throughout Vietnam.

**Results:** The results show that the impacts varied by provinces. They were classified in 4 groups: *positive impact, positive impact without sustainability, possibly positive impact, no or negative impact* of the LPCID. The meta-analysis indicated that the country-level impact of the LPCID became significant at 11 months after the LPCID took effect, with a decrease in level of diarrhoea of 9.7% (coefficient, -0.097; 95%CI: -19.1-(-0.002)) and a permanent downward trend of diarrhoea at a rate of 1.1% per month (coefficient, -0.011; 95%CI: -0.02-(-0.003)); whereas the trend in diarrhoea before the LPCID took effect was unchanging (coefficient, 0.002; 95%CI, 0-0.004). At 12, 24, 36, 48, and 60 months following the LPCID implementation date the levels of diarrhoea decreased by 10.9% (coefficient, -0.109; 95%CI: -0.203-(-0.015)), p<0.01, 21.8% (coefficient, -0.218; 95%CI: -0.338-(-0.098)), p<0.01, 31% (coefficient, -0.31; 95%CI: -0.474-(-0.145)), p<0.01, 46.8% (coefficient, -0.468; 95%CI: -0.667-(-0.27)), p<0.01, 48.2% (coefficient, -0.482; 95%CI: -0.708-(-0.256)), p<0.01) respectively.

**Discussion & Conclusion:** The findings of this study reveal the effectiveness of the LPCID in reducing diarrhoea incidence in Vietnam. However, further studies should be conducted to better understanding the cost-effectiveness, acceptability, and sustainability of each component of the LPCID.
1.0 Introduction

Diarrhoea is one of the leading causes of morbidity and mortality in developing countries [1-4]. It has been estimated that a billion episodes of diarrhoea and 3 million deaths in children under 5 years are attributed to infectious gastroenteritis, almost all of them in developing countries [5, 6]. In developed countries where enormous benefits have been realised from substantial improvement in hygiene, sanitation, health, and nutrition, so the occurrence of severe disease is mostly confined to biological agents capable of adapting to or resisting these changes. Whereas in developing countries such prevention measures are largely hindered by climatic, social, and economic factors with the result that diarrhoea related morbidity is still high [6]. Therefore, health policies that integrate the multiple solutions and better multi-sectoral involvement and coordination might be expected to play a crucial role in prevention and control of diarrhoeal diseases in developing countries. Jamison et al (2006) recommended that the policy and priorities for diarrhoeal disease controls in developing countries should integrate new products and tools which could significantly improve the efficacy of the interventions such as vaccines, development of new treatment strategies, and provision of clean water and control human waste. In Vietnam, despite significant improvements in drinking water sources and sanitation facilities in recent years [7], rapid population growth, lack of investment in health and aging water and sewage infrastructure have exposed more residents to increasingly polluted water [8, 9]. In addition, exposure to wastewater and excreta during agricultural activities contribute significantly to the risk of diarrhoea among residents in rural areas[10]. As a consequence, management of diarrhoea has become more challenging in both developed urbanized and resource-limited rural settings [11]. Furthermore, such rapid social and economic development, resulting in speedy urbanization, changes in methods for animal production, food marketing systems, food consumption habits, and food regulations also cause major impacts on foodborne diarrhoea due to food poisoning [12]. As reported by provincial preventive medicine centres, diarrhoea is still the most widespread infectious disease throughout Vietnam. To address morbidity and mortality from infectious disease including diarrhoea, the Vietnamese government enacted the
Law on Prevention and Control of Infectious Diseases (LPCID) in July 2008 [13]. This law comprises collective actions and regulations to strengthen systematic prevention and control measures of infectious diseases. Nevertheless, no evaluation of the impact of the LPCID has been conducted.

This study aims to evaluate the 5-year impact of the Law on Prevention and Control of Infectious Diseases on diarrhoea control in Vietnam.

2.0 Methods

2.1 Data Collection:

The Law on Prevention and Control of Infectious Diseases (LPCID) was promulgated by the National Assembly of Vietnam on November 2007 and took effect on 1 July 2008. The LPCID includes a collection of strategies and actions organized in six chapters (General Provision, Prevention of Infectious Diseases, Border Quarantine, Combating Epidemics, Conditions for Assuring Prevention and Control of Infectious Diseases, and Implementation Provisions) comprising 64 articles that cover a wide range of actions for infectious disease prevention and control (Supplement 1). This study used July 2008 as the segmented time for evaluating impact of the LPCID on diarrhoea control.

Monthly counts of diarrhoea from January 2000 to December 2015 were obtained from the disease surveillance reports of provincial Preventive Medicine Centres (PMC) throughout Vietnam. The definition of diarrhoea from the World Health Organization (WHO) is a disease of an infection in the intestinal tract, which can be caused by a variety of bacterial, viral and parasitic organisms. The typical symptom of diarrhoea is the passage of three or more loose or liquid stools per day or more frequent passage than is normal for the individual [14]. The LPCID stipulates that diarrhoea is one of the infectious diseases for which physicians in hospitals and clinics must report diarrhoeal cases to the local health authority within 24 hours. All hospitals and clinics report weekly counts of new cases to the provincial PMCs at the same levels. Then, PMCs analyse the reported data for the purpose of disease prevention at the provincial level [13]. Therefore, it is believed that the monthly counts of diarrhoea are consistent and representative for the provinces over the study period.
Daily meteorological data (temperature and humidity) were obtained from the provincial hydro-meteorological stations or the closest airport weather stations from 1st January 2000 to 31st December 2015, and then these daily data were collapsed into monthly average values for data analysis. The data on populations were obtained from Vietnam General Statistics Office [15] and Health Statistic Yearbook [16].

2.2 Statistical Analysis

Firstly, an interrupted time series design [17], which is considered the strongest quasi-experimental method for evaluating longitudinal effects of policies and interventions, was applied using a segmented regression analysis (Equation 1) to estimate the impact of LPCID on diarrhoea control for each province. We checked the goodness-of-fit of the overall interrupted time-series model (ITS) using the average incidence rates as the dependent variable, and continuous time variables (before and after the law effective date) and the categorical variable (0,1) for the law effective data as an independent variable. We used R-squared and root-mean-square error (RMSE) to evaluate the goodness of fit of the ITS model. The study suggested that at least 100 observations of time series are required to achieve an acceptable level of variability of the estimate and to maximize statistical power [18]. Therefore, only provinces which provided data of at least 100 observations with a minimum of 24 months prior to the implementation of LPCID were included in the analysis. The percentage change in level (the y-intercept) and trend (the slope) of diarrhoea were estimated for each month over the 60 months after the LPCID took effect. In order to model the effects of multi-period interventions and to avoid incorrect specification of intervention effects, we excluded from the analysis monthly diarrhoea cases that occur during the lag or ‘during the law’ period. For example, the diarrhoea cases for month 0 and 1 were excluded when estimating the impact of LPCID on month 3. The climate factors (temperature and humidity), which are potential confounding factors and have been reported as having a non-linear effect on diarrhoea[19, 20], were controlled using a natural cubic spline function with 3 degrees of freedom. The seasonal trend of
diarrhoea was also controlled using the dummy variables for each month of the year. The population size was also adjusted as an offset in the model. Equation 1 identifies the model fitted.

\[ Y_t \sim \text{Poisson}(\mu_t) \]

\[ \ln(\mu_t) = \beta_0 + \beta_1 \text{time}_t + \beta_2 \text{LPCID}_t + \beta_3 (\text{time after LPCID})_t + s(\text{Temperature}, 3df) + s(\text{Humidity}, 3df) + \gamma \text{MOY} \]  

Equation 1

where, \( Y_t \) is the mean of monthly counts of diarrhoea; \( \text{time}_t \) is a continuous variable indicating time in months at time \( t \) from the start of the observation period; \( \text{LPCID}_t \) is an indicator for time \( t \) occurring before (LPCID=0) or after (LPCID=1) the LPCID’s implementation; \( \text{time after LPCID} \) is a continuous variable counting the number of months after the LPCID’s implementation at time \( t \); \( s \) is natural cubic spline functions of monthly temperature and humidity with 3 degrees of freedom; and \( \text{MOY} \) is month of a year. In this model, \( \beta_1 \) estimated the change in the monthly diarrhoeal cases that occurs with each month before the LPCID implementation (i.e. baseline trend); \( \beta_2 \) estimated the level change in the mean of monthly diarrhoeal cases immediately after \( t \) months following the LPCID’s implementation date; and \( \beta_3 \) estimated the change in the trend in the mean of monthly diarrhoeal cases after the LPCID’s implementation, compared with the monthly trend before the LPCID’s implementation.

Secondly, we used meta-analysis to estimate the pooled estimates of the country-level impact of LPCID on diarrhoea control throughout Vietnam. Because the impact of the LPCID might vary across provinces due to variability of population and socio-economic factors, resulting in considerable heterogeneity of findings, a random-effect meta-analysis was applied to calculate within-province and between-province variation and generate pooled estimates of changes in level and trend (% change) of diarrhoea. The pooled estimates were calculated for each month after the LPCID implementation date over 60 months. Heterogeneity between provinces was quantified by the coefficient of inconsistency \((I-Squared)\) which describes the percentage of total variation across provinces that is due to heterogeneity [21].

3.0 Results
Thirty two provinces provided valid data for data analysis (Figure 1-A). These provinces are located and representative for eight ecological regions throughout Vietnam with a total population of 48,093,000 (Supplement 1). A total number of diarrhoeal cases of 5,017,961 over a time-span of 5,289 months were recorded for 32 provinces. The number of months involved in the evaluation was ranged from 106 to 192 with an average of 165 months/ per province, of which the shortest time-span was from January 2006 (30 months prior to the LPCID) to October 2014 (76 months after the LPCID). The average monthly incidences of diarrhoea varied widely across provinces from 6 to 267 cases/ 100,000 persons across provinces (Figure 1-A). The three top provinces with highest incidences of diarrhoea were observed in the Northern mountainous region (Ha Giang province, 143.3/ 100,000 person-months), Southern Highland (Kontum province, 267.3/100,000 person-months), and Mekong Delta region (Ben Tre province, 146.9/100,000 person-months). In terms of temporal distribution, the monthly incidence of diarrhoea, which was averaged from the 32 provinces, was decreased sharply after the LPCID implementation date (July 2008) (Figure 1-B).

The goodness-of-fit test indicates that the overall IST model was good fit to predict the diarrhoeal incidence rates (R-squared, 0.77; RMSE, 8.62; Figure 1B). For province-level impact, we classified provinces in four main groups (Figure 2). Group 1 comprises 18 provinces where we identified a positive impact of the LPCID reflected by a steep decrease and a permanent downward trend in diarrhoea after a number of months following the LPCID implementation; whereas, no change or increased trend in diarrhoea was observed before that date in these provinces. The time-span for significant impact of the LPCID ranged from 1-39 months and the changes in level of diarrhoea at the start point varied from 2.9% to 39% across these 18 provinces. Group 2 comprises 2 provinces which had a positive impact without sustainability of the LPCID reflected by an immediate steep decrease in diarrhoea but an upward trend in diarrhoea after a number months following the LPCID implementation while no change or increased trend in diarrhoea was observed before that date. In these two provinces, the level of diarrhoea decreased 7.9% after four months and 15.8% after one month following the LPCID implementation, but then the trend increased at the rate of
0.5% and 1.8% per month respectively. **Group 3** comprises 7 provinces which had a possible positive impact of the LPCID reflected by an immediate steep decrease and a permanent downward trend in diarrhoea after a number of months following the LPCID implementation date. However, a decreasing trend in diarrhoea was also observed before that date in these provinces. **Group 4** comprises 5 provinces where no impact or negative impact of LPCID was observed reflected by a steep increase and permanent upward trend in diarrhoea after a number of months following the LPCID implementation date regardless of what the trend in diarrhoea that was observed before that date in these provinces. Lang Son province and Ho Chi Minh City showed statistically significant increases in both change and trend of diarrhoeal rate following the law effective date. This might be attributable to the large amount of tourists to these settings. The details of the changes in level and trend of diarrhoea by provinces and months are reported in Supplement 3.

For the country-level impact, Figure 3 shows the pooled estimates of changes in level of diarrhoea which indicates a steep decrease in diarrhoea over the months following the LPCID implementation date, whereas, the trend in diarrhoea before that date was not changed (coefficient, 0.002; 95% CI, 0.004; p, 0.1). The pooled estimates of the changes in level and trend of diarrhoea indicated that the significant impact of the LPCID started at Month 11 following the LPCID implementation date with a decrease in level of diarrhoea of 9.7% (coefficient, -0.097; 95% CI: -0.191 to -0.002, p<0.01) and a permanently downward trend in diarrhoea at a rate of 1.1% per month (coefficient, -0.011; 95% CI: -0.02 to -0.003, p<0.01). Figure 4 presents the patterns of change in level and trend in diarrhoea by years following the LPCID implementation date in comparison with the baseline trend. At 12, 24, 36, 48, and 60 months following the LPCID implementation date the levels of diarrhoea decreased by 10.9% (coefficient, -0.109; 95% CI: -0.203 to -0.015, p<0.01), 21.8% (coefficient, -0.218; 95% CI: -0.338 to -0.098, p<0.01), 31% (coefficient, -0.31; 95% CI: -0.474 to -0.145, p<0.01), 46.8% (coefficient, -0.468; 95% CI: -0.667 to -0.27, p<0.01), 48.2% (coefficient, -0.482; 95% CI: -0.708 to -0.256, p<0.01) respectively. Meanwhile a permanent downward trend was observed with a rate of 1.1%, 1.3%, 1.5%, 1.6%, and 1.6% following the 12, 24, 36, 48, and 60-month post-LPCID.
respectively. The pattern of changes in diarrhoea at Month 60 was similar to that at Month 48 (the figure is not shown). The forest plots of the pooled estimates computed from meta-analysis by months are presented in Supplement 4A-E.

4.0 Discussion

This is the first study to quantitatively evaluate the impact of a national law on prevention and control of infectious diseases in Vietnam using interrupted time-series (ITS) method that is considered as a valuable study design for evaluating the effectiveness of population-level health interventions ranging from clinical therapy to national public health legislation [22]. The study used a quasi-experimental interrupted-time series approach and meta-analysis to examine the impact of the Law on Prevention and Control of Infectious Diseases (LPCID) on diarrhoea control. The evaluation was conducted at a province-level and country-level with the involvement of multiple provinces representing different ecological regions throughout Vietnam. The results indicate that the impacts of the LPCID on the diarrhoea control varied across provinces with different time-spans for reductions and differing patterns of monthly diarrhoea cases. This might reflect differential implementation of the LPCID due to differences in resources capacities among provinces. However, the overall result provides a basis evidence on the impact of the LPCID in reducing diarrhoea at the country-level, and this reduction was detected statistically a year following the LPCID implementation date. A reduction approximately 50% in diarrhoeal rate was observed after 4 years after the LPCID implementation date.

The LPCID implemented in July 2008 covers a wide range of collective actions and regulations to prevent and control infectious diseases in Vietnam, including: education, sanitation, vaccination, surveillance, border quarantine, and epidemic control. The findings of this study suggest the effectiveness of these multiple interventions on diarrhoea control which are consistent with the findings of previous studies. A meta-analysis by Fewtrell et al [23] indicated that hygiene education could reduce 28% of diarrhoeal rate (pooled estimate of RR, 0.72; 95%CI: 0.63-0.83) in community
population, and other studies [22, 24-26] suggested that Information, Education and Communication (IEC) programs for food hygiene and food safety especially have a significant impact in reducing diarrhoea. For instance, Takanashi et al (2013) found that IEC could improve food hygiene and food safety behaviour up to 33% and 88% respectively, resulting in a 21.6% decrease in childhood diarrhoea in Vietnam. Nevertheless, these studies on the effectiveness of IEC focused more on the children than on adults, who need to be further studied in the future. The implementation of hygiene and sanitation intervention has been found to make significant contributions to diarrhoea control. The study by Fewtrell et al (2005) demonstrated that hygiene interventions for reducing of contamination of hands, food, water, and fomites could cause a reduction of up to 45% in diarrhoea (RR: 0.56; 95%CI: 0.33-0.93) while the sanitation programs, water supply and water quality were associated with 32% (RR, 0.68; 95%CI: 0.53-0.87), 25% (RR, 0.75; 95%CI: 0.62-0.91), and 31% (RR, 0.69; 95%CI: 0.53-0.89) reduction in diarrhoea, respectively [23]. These findings are supported by other studies that have reported significant impacts of hygiene and sanitation programs in reducing diarrhoea [27-32]. However, which intervention program is better than others, and whether multiple interventions are more effective than interventions with a single focus are still open questions for further studies.

In terms of vaccination, several studies [33-36], which focused on rotavirus vaccination, indicated that a national rotavirus vaccination program could be a cost-effective measure to effectively reduce deaths, hospitalizations, and outpatient visits due to rotavirus diarrhoea. Karafillakis et al (2015) found that vaccine effectiveness against rotavirus-related healthcare utilization ranged from 68% to 98% and made reductions in rotavirus hospitalizations ranged from 65% to 84% across Europe [33]. Likewise, Atherly et al (2012) projected that rotavirus vaccination could prevent 2.46 million childhood deaths and 83 disability-adjusted life years (DALYs) from 2011 to 2030 in low-income countries, and the authors indicated that vaccination is most cost-effective and has the greatest impact in regions with high rotavirus mortality [37]. A similar study conducted by Kim et al (2009) suggested that rotavirus vaccination would not completely protect young
children against rotavirus infection due to the nature of vaccine immunity but would effectively reduce the number of severe cases of rotavirus gastroenteritis in Vietnam by about 67% over the first 5 years of life [38]. So far, no study in effectiveness of improvement of the systems for surveillance, border quarantine, and epidemic preparedness on diarrhoea control has been reported in developing countries. Further studies should be conducted to examine the efficacy of these measures on diarrhoea control.

This study has some limitations. First, complete data on diarrhoea were not provided from all of 64 provinces throughout Vietnam due to the inconsistent quality of surveillance systems across provinces. This might be a bias because the provinces provided incomplete data or did not provide data might implement LPCID in a more incomplete way. However, the 32 provinces that did provide sufficient data were adequate to represent all ecological regions and socio-economic status of Vietnam (Figure 1). Second, the time-spans for health outcome data prior to the LPCID implementation date were not the same across all provinces. Although this study only selected the provinces which provided at least 24 months of data, the results of time-series regression analysis can vary depending on which sets of time points are used. However, this study used random-effect meta-analysis to take into account heterogeneity of the findings from individual provinces. Third, the routine data did not include households’ characteristics, socio-economic factors (e.g. gender, wealth), and event-related issues (e.g. disruption to normal water/sanitation services during flooding events is associated with diarrhoeal [39]), so this limited a consideration of the potential confounding effects of these factors on the impact of the LPCID. Further studies may need to be conducted to examine the roles of individual households’ characteristics and socio-economic factors on the effectiveness of the LPCID. Finally, how well the law was implemented in each province and which parts of the LCPIID were more effective than others and why; and how the LCPIID is accepted and its sustainability are beyond the scope of this study and remain important questions to be answered by future study. Qualitative research methods will be useful to help investigate further these why and how questions.
5.0 Conclusions

This study used a segmented intervention analysis which provides an appealing methodological framework to assess the impact of policy changes on outcomes using data routinely monitored by routine health surveillance systems from many jurisdictions. The results of this study revealed the significant impact of the Law on Prevention and Control of Infectious Diseases in reducing diarrhoea incidence in the majority of provinces included in the analysis, and this positive impact was also observed at the country level throughout Vietnam. These findings demonstrate the effectiveness of collective actions and regulations on infectious disease control in developing countries. Further studies should be conducted to better understanding the cost-effectiveness, acceptability and sustainability of each component of the LPCID in Vietnam.

**Competing interests:** None declare
References

**Figure 1.** The spatial and temporal distribution of diarrhoea rates

**Figure 2.** The changes in level and trend of diarrhoea rate following the law effective date by provinces

**Figure 3.** The pooled effect sizes of changes in level of diarrhoea incidence following the law effective date by months

**Figure 4.** The pooled effect sizes of changes in level and trend of diarrhoea incidence following the law effective date by years