中文摘要

本論文之目的為提供一整合性數學模式以描述室內呼吸性傳染病麻疹與流感之傳輸動態、控制策略模擬及成本效益分析。本架構之基礎資料包括季節性流感之流行病學資料與麻疹疫苗前後之全國/山區/鄉村/都市之血清流行病學資料。第一部分，本研究以三個相異之接觸矩陣（Who Acquire Infection From Who，WAIFW 描述在不同年齡族群中及不同年齡族群之間的麻疹傳染率，量化疫苗前後因年齡而異之感染力與基本再生數（Basic reproduction number，R_0），而後，結合一標準之易感–暴露–感染–復原（Susceptible-Exposed-Infective-Recovery，SEIR）模式，以一簡易之一階常微分方程式，明確地模擬麻疹疫苗施行後，傳染發生之族群動態。

其次，本研究利用一機制模式Wells-Riley數學方程式推測學校孩童於通風空間中之流行性感冒感染機率，依據通風空間中之環境影響因子（如空間大小與通風率）及傳染者之影響因子(如人體呼吸率與暴露於通風空間中之時間)，可推測出季節性且因年齡而異之感染風險與基本再生數。本研究亦結合Wells-Riley數學方程式與競爭風險（Competing-risks）模式，量化學校孩童暴露於學校之環境下，採取控制策略對於室內環境流感發生之衝擊，探討以室內通風為基礎之工程控制與個人保護方法之影響，更進一步研擬以Von Foerster方程式加以量化公共衛生策略包含流感疫苗與隔離政策施行之衝擊。因此，藉由上述之Wells-Riley數學方程式、Competing-risks模式及Von Foerster方程式之整合，可建立一關鍵之$R_0-\theta$控制曲線以最佳化研擬控制策略之衝擊，其中θ表示未發生症狀而可傳染的期間除以可傳染總時間長度之比例。

第三部份，本研究發展一套以成本效益為基礎之整合性數學模式，以模擬季節性流感之發生。針對工程控制方法(如室內通風、紫外光殺菌燈及高效率顆粒過濾網)、個人保護方法(如口罩與洗手)及公共衛生策略(如疫苗施行與隔離政策)之控制效率與成本加以整理蒐集以利進行成本-效益分析，並以資源使用最小化、平均每人負擔之成本功效最大化為目標，建立出因應季節性變異之最佳化流感控制策略。

本研究結果指出區域性或全國性之疫苗計畫可大幅降低麻疹流行之主要衝擊。成本-效益分析可利用於評估多種整合性控制策略對於季節性流感之衝擊，本研究可提供一個完整且已量化之麻疹與流感傳輸動態，藉由結合室內呼吸性傳染病之傳輸機制、控制策略之衝擊研擬，與成本-效益分析之整合性方法，對於預測學校孩童感染流感將會是個強而有力的工具。

關鍵字：室內呼吸性傳染病；傳輸動態；成本–效益；易感–暴露–感染–復原模式；控制策略；流行性感冒；麻疹；基本再生數

ABSTRACT

The objective of this dissertation is to provide an integrated relevant mathematical model for describing the transmission dynamics, control measures modeling, and cost-effectiveness analysis for indoor respiratory infections including measles and influenza. The empirical evidence of proposed framework is based on the seasonal epidemiological data of influenza and robust age-stratified seroepidemiological data of measles for pre/post-vaccination and setting of nationwide/mountain/rural/urban. In the first phase, three contact patterns of "who acquire infection from who" (WAIFW) matrices are employed to characterize the transmission rate within and between each age group and subsequently the parameters of age-dependent force of infection and age-dependent basic reproduction number (R_0) for measles can be quantified. A standard susceptible-exposed-infected-recovery (SEIR) structure can model straightforwardly the dynamics of measles vaccination by using a simple parameterized set of differential equations.

Secondly, Wells-Riley mathematical model is used to predict the influenza infection risk in terms of environmental factors (e.g., room size and ventilation rate) and host factors (e.g., breathing rate and exposure time) and to estimate seasonal-specific age-dependent risk of infection and R_0. This study integrates the Wells-Riley mathematical equation and competing-risks model to quantify the impact of combination efforts of indoor air-based engineering and personal protection control measures in containing pandemic influenza within an elementary school. Public health interventions including vaccination and isolation are modeled based on the Von Foerster equation for schoolchildren infected influenza. Then, a critical $R_0 - \theta$ control line constructed by integrating the Wells-Riley equation, competing-risks model, and the Von Foerster equation, is used to prioritize control measure efforts.

The symbol θ , asymptomatic proportion, can be defined as the ratio of the asymptomatic infection over the summation of symptomatic and asymptomatic infection.

In the third phase, an integrated mathematical model linking with the cost-effectiveness-based control methods is developed for preventing from seasonal influenza in an elementary school. The costs and effectiveness of engineering control measurers (ventilation, ultraviolet germicidal irradiation, high-efficiency particulate air filter), personal protection (respiratory masking and handwashing), and public interventions (vaccination and isolation) were collected to perform the cost-effectiveness analysis to minimize the waste of resource and to maximize the health per dollar spent because the seasonal variation in disease transmission may play an important role on modeling the optimal control measures on influenza.

In the present study, the results indicate that the mass regional or nationwide vaccination programmes could greatly reduce the potential for a major measles epidemic. The cost-effectiveness analysis is useful for evaluating the multiple control measures on seasonal influenza. This work can provide a quantitative understanding of the transmission dynamics of measles and influenza. The proposed integrated approach, by employing the mechanism of transmission of indoor respiratory infection, the impact of infectious control programs, and the cost-effectiveness analysis, is a powerful tool for risk profiling prediction of pandemic influenza among schoolchildren.

Keywords: Indoor respiratory infections; Transmission dynamics; Cost-effectiveness; Susceptible-exposed-infected-recovery (SEIR) model; Control strategy; Influenza; Measles; Basic reproduction number (R_0)