Effect of lifestyle factors on risk of mortality associated with influenza in elderly people

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KEY MESSAGES

1. Never-smokers had significantly lower risk of all-cause and cardiorespiratory mortality secondary to influenza than ex-smokers and current-smokers.
2. Regular and moderate exercisers had lower risk of all-cause and cardiorespiratory mortality secondary to influenza than those who had a sedentary lifestyle.
3. Consuming less alcohol was not associated with reduced mortality risk associated with influenza.
4. Community-dwelling older people in Hong Kong should be encouraged to maintain a healthy lifestyle in order to lower the mortality risk from influenza infection.

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Introduction

Influenza poses a major health hazard in terms of mortality and morbidity, particularly in elderly people. It is controversial whether vaccination can effectively reduce the incidence of influenza infection and the risk of hospitalisation and mortality in elderly people.[1] The time delay with respect to vaccine production results in an occasional mismatch between vaccines and circulating strains of influenza. Annual vaccination campaigns are also hampered by concerns over potential adverse events of vaccines.[2] Therefore, preventive approaches such as improving personal hygiene and maintaining a healthy lifestyle should be encouraged.

Effects of smoking, drinking alcohol, and physical exercise on infection risks of influenza have been studied. This study assessed the modification effects of smoking, exercise, and alcohol consumption on the mortality risk from influenza in a large elderly cohort with a follow-up period of nearly 12 years.

Methods

This study was conducted from September 2009 to August 2010. From May 1998 to December 2001, 66 820 older people (aged ≥65 years) living in the community were recruited from 18 elderly health centres (EHCs) managed by the Department of Health. Data on the participants' lifestyle (history of smoking, exercise frequency, and alcohol consumption) and socioeconomic status (housing type, education, and monthly expenditure) were collected by trained nurses and doctors using a standardised questionnaire. The participants' health status was assessed using comprehensive clinical examination, and any chronic conditions were recorded at the first visit.

Smoking status was categorised as never-, current-, and ex-smokers, where ex-smokers were those who had ever smoked but had stopped for ≥1 year. Alcohol consumption status was categorised as never-, ex-, and social/regular drinkers, where never drinkers were those who had never drunk alcohol, ex-drinkers were those who had drunk alcohol previously, and social and regular drinkers were those who drank alcohol on <4 and ≥4 days per week, respectively. Exercise was categorised as sedentary, moderate-, and frequent-exercise based on the self-reported frequency and duration of regular exercise, where sedentary was defined as not doing any exercise at all, moderate exercise was defined as not doing exercise every day or for <30 minutes each time, and frequent exercise was defined as doing exercise for >30 minutes every day.

The death registration data were linked to the cohort baseline using the Hong Kong identity card number. Participants with an unknown date of death (n=194) were excluded, and the final sample included 66 626 elderly people. All participants with unknown vital status were censored on 2 January 2010, and those who died from accidents were censored on the reporting dates of death in their death registration records. Influenza and respiratory syncytial virus (RSV) virology data were obtained from the microbiology laboratory of Queen Mary Hospital. The weekly proportions of specimens

positive for influenza (or RSV) were used as a proxy for influenza (or RSV) virus activity. Meteorology data of temperature and relative humidity were obtained from the Hong Kong Observatory.

Statistical analysis

Time-dependent Cox proportional hazards models were used to estimate the hazard ratio of influenza-associated mortality for all-cause and chronic respiratory disease (CRD) mortality. To adjust for confounding seasonal factors, time-dependent variables for long-term and seasonal trends of mortality, meteorological factors, weekly average concentrations of ambient air pollutants, and co-circulation of RSV were included in the models with 'week' as the unit of time. Age, sex, education, housing type, co-morbidity score, smoking, exercise, and alcohol consumption were added into the models as time-independent variables. Effect modification of smoking, alcohol consumption, and exercise was assessed by the interaction terms of influenza virus activity and dummy variables for each lifestyle factor in the interaction models. The statistical significance of interaction terms was assessed by likelihood ratio tests between models with and without interaction terms. Stratified analyses were also conducted for each stratum of smoking, alcohol consumption, and exercise no matter whether their interaction terms were significant in the interaction models. Influenza-associated excess risk of mortality for each stratum of lifestyle factors was measured by the percentage change in the hazard associated with every 10% increase of influenza virus activity. A P value of <0.05 was considered statistically significant.

Results

The interaction between influenza virus activity and each of the three lifestyle habits in terms of all-cause

TABLE. Difference in excess mortality risks (in %) associated with 10% increase in influenza virus activity relative to the reference groups

Parameter	Per 10% increase in influenza activity					
	Both sexes	P value*	Men	P value*	Women	P value*
All-cause mortality						
Smoking						
Never	0	0.657	0	0.643	0	0.126
Ex	2.1 (-2.5 to 6.9)		2.2 (-4.8 to 9.7)		3.4 (-4.6 to 12.1)	
Current	1.4 (-4.4 to 7.5)		-1.2 (-9.0 to 7.3)		11.3 (0.0 to 23.8)	
Alcohol consumption						
Never	0	0.619	0	0.735	0	0.812
Ex	1.8 (-3.8 to 7.7)		2.2 (-5.0 to 10.1)		2.8 (-7.3 to 14.0)	
Social/regular	-1.8 (-7.1 to 3.9)		-1.1 (-8.0 to 6.4)		-1.8 (-11.5 to 9.1)	
Exercise						
Sedentary	0	0.139	0	0.167	0	0.180
Moderate	-3.0 (-8.5 to 2.8)		-7.7 (-15.3 to 0.6)		0.7 (-7.0 to 9.1)	
Frequent	-5.4 (-10.6 to 0.1)		-6.4 (-13.7 to 1.5)		-4.4 (-11.6 to 3.3)	
Chronic respiratory disease mortality						
Smoking						
Never	0	0.751	0	0.393	0	0.051
Ex	-1.7 (-7.8 to 4.9)		-5.5 (-14.5 to 4.3)		1.1 (-9.6 to 13.1)	
Current	1.9 (-6.6 to 11.1)		-7.4 (-18.0 to 4.5)		21.1 (4.2 to 40.8)	
Alcohol consumption						
Never	0	0.020	0	0.174	0	0.056
Ex	5.4 (-2.4 to 13.8)		2.9 (-6.9 to 13.8)		13.0 (-1.8 to 29.9)	
Social/regular	-9.1 (-16.6 to -0.9)		-7.8 (-17.3 to 2.8)		-12.7 (-26.3 to 3.6)	
Exercise						
Sedentary	0	0.046	0	0.120	0	0.131
Moderate	4.0 (-4.4 to 13.0)		-2.1 (-13.3 to 10.6)		9.6 (-2.3 to 23.1)	
Frequent	-4.0 (-11.6 to 4.3)		-9.8 (-19.8 to 1.5)		(-9.4 to 14.1)	

* Likelihood ratio tests for interaction between influenza and lifestyle factors on the mortality effects

and CRD mortality was analysed. Smoking was marginally significantly associated with all-cause mortality in women (P=0.051), whereas alcohol consumption (P=0.020), and exercise (P=0.046) were significantly associated with CRD mortality in both sexes combined (Table).

For every 10% increase in influenza virus activity in the community, the risk of CRD mortality increased by 25.8% (P<0.05) in female current smokers, which was more than 10-fold higher than that of female never- and ex-smokers. Results were similar for all-cause mortality in female current smokers with a smaller increase in mortality risk of 16.3%. However, the excess risk of mortality was not significant among the three male smoking subgroups, but male ex-smokers tended to have a higher mortality risk attributable to influenza than never-smokers. For both sexes combined, ex-smokers had a similar excess risk of influenza-associated CRD mortality as current smokers (Fig). Both female and male ex-alcohol drinkers had significantly higher excess risk of all-cause and CRD mortalities associated with influenza, but the excess risk of mortality was significant only in the male and combined sex groups. Never drinkers and social/regular drinkers had similar excess risk of all-cause mortality, and none of their estimates were significant (Fig). The excess risk of mortality

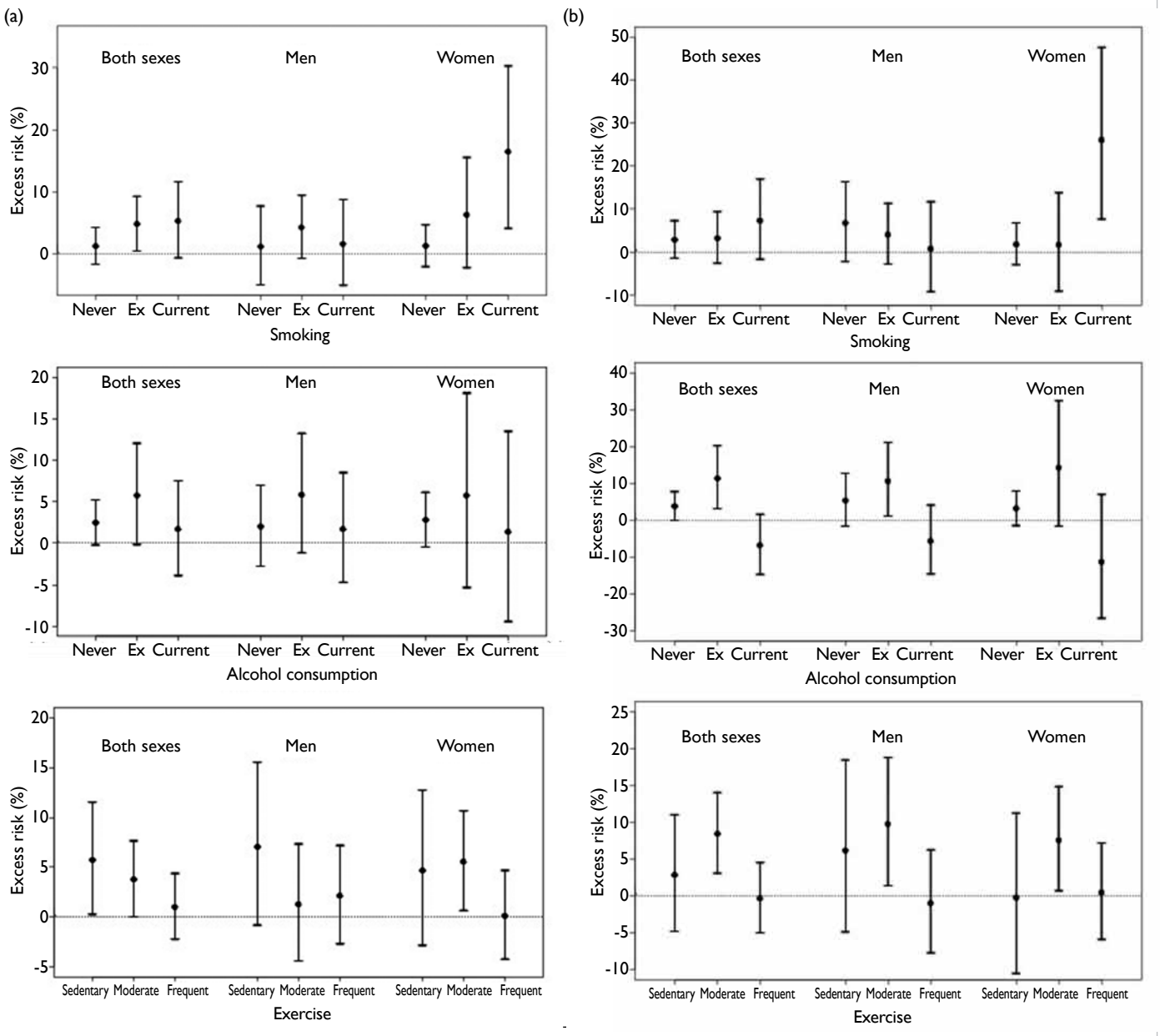

FIG. Excess mortality risks (in %) associated with 10% increase in influenza virus activity, stratified by the sex and lifestyle groups: (a) all-cause mortality and (b) chronic respiratory disease mortality

associated with influenza was lower for frequent exercisers than for the other two groups, with the exceptions of all-cause mortality in men and CRD mortality in women. Participants who took moderate exercise had lower influenza-associated excess risk of all-cause mortality than those who had a sedentary lifestyle for the men and combined sex groups, but had consistently higher excess risk of CRD mortality among both men and women (Fig).

Discussion

Mortality risks associated with influenza were much higher for current smokers than for those who had never smoked among both female and male older people. Smoking can cause structural changes in respiratory epithelial cells and suppress both cell- and humoral-mediated immunity responses against infections.[3]

Regular moderate exercise is associated with reduced viral load and increased serum level of inflammatory factors in mice infected with influenza viruses, but the association between exercise and respiratory infections has not been established.[4] Our study provides further evidence for a potential beneficial effect of occasional and frequent exercise in lowering the mortality risks of influenza infection among older people. Although the intensity of exercise taken by each participant in the moderate and frequent exercise groups was unknown, the type of exercise suggested that nearly 90% were exercising normally at low to moderate intensity such as stretching, slow walking on level ground, and Tai Chi. Further studies using a standardised exercise protocol combined with accurate measurement for energy expenditure and laboratory tests for respiratory pathogens are warranted.

Chronic exposure to ethanol increases the susceptibility of mice to infection from respiratory viruses by suppressing the cellular response and altering the immune cytokine levels.[5] However, in our study, excess risks for CRD and all-cause mortality attributable to influenza were lower among the social/regular drinkers than among the ex-drinkers and never drinkers. A protective effect (despite not being significant) was observed for social/regular drinkers for CRD mortality. In these participants, only 456 (2%) men had ≥3 drinks per day and 64 (0.1%) women had ≥2 drinks per day. Therefore, it seems that few of the EHC members were heavy drinkers, which could explain why we did not observe an adverse effect of alcohol consumption for mortality risk associated with influenza. Furthermore, we did not consider the heterogeneous effects of the different types of alcoholic drinks due to lack of such data.

There were limitations to our study. First, the vaccination history of each participant was not known, which could bias the estimates of influenza effects. Second, estimates for influenza effects were based on modelling the association between influenza activity and incidence of death, ie whether death rates increased along with increased influenza virus activity. However, it would be unrealistic to make a laboratory diagnosis for each suspected influenza case given the cost of laboratory tests. Third, the participants were recruited through their voluntary visits to the EHC, therefore they tend to be healthier and more health conscious than those dwelling in the community but never visited an EHC. Nevertheless, the small Cohen's effect sizes show that our cohort is representative in lifestyle and socioeconomic aspects. Last, all the lifestyle data were collected at baseline during the participants' first visit to the EHC. Misclassification bias could have been introduced if some participants had changed their habits during the follow-up period.

Conclusion

Never-smokers had a lower mortality risk attributable to influenza than ex- and current-smokers. Frequent exercisers also had a lower risk than sedentary people. However, the beneficial effects of consuming less alcohol were not conclusive. Taken together, maintaining a healthy lifestyle is associated with significant reduction of the mortality risks attributable to influenza.

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