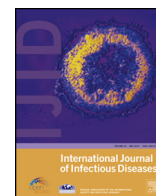




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Short Communication

Seasonal synchrony in incidences of common infectious diagnoses in early childhood among neighbouring regions

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SUMMARY

Objectives: Information on seasonal synchrony of influenza activity between neighbouring regions has been found useful for planning infection control measures. Seasonal synchrony of other infectious diseases is less known. We describe the seasonality and seasonal synchrony of three common childhood infectious diagnoses among three regions in Taiwan.

Methods: A large, nationally representative sample of young children ($N = 128\,651$, age 0–4 years) was used to estimate the monthly incidences of acute respiratory infection, acute intestinal infection, and herpangina and hand, foot, and mouth disease (HFMD) in three regions of Taiwan between 2000 and 2005. Seasonality of monthly incidences was indicated by year-on-year intra-class correlations (ICCs). Between-region ICCs were used to describe seasonal synchrony of incidences between regions.

Results: We found evidence of seasonality in all three infectious diagnoses ($p < 0.05$). Seasonal synchrony among the three regions was highest for acute respiratory infection (between-region ICC 0.91, 95% confidence interval (CI) 0.87–0.94), followed by herpangina and HFMD (between-region ICC 0.85, 95% CI 0.80–0.90), and acute intestinal infection (between-region ICC 0.69, 95% CI 0.59–0.79).

Conclusions: We found strong evidence of seasonal synchrony in the incidences of acute respiratory infection, acute intestinal infection, and herpangina and HFMD between three neighbouring regions of Taiwan. An understanding of these disease patterns may inform future infection control measures.

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1. Introduction

Information on seasonal synchrony of influenza activity between neighbouring regions or interconnected cities has been found useful in identifying patterns of viral spread^{1,2} and facilitating control measures.² Seasonal synchrony of other infectious diseases is less described.³ Here we demonstrate the seasonality and seasonal synchrony of three common childhood infectious diagnoses among three regions in Taiwan.

2. Methods

The Taiwan Longitudinal National Health Insurance Research Dataset 2005 is a very large (one million), random, and anonymous

sample of the Taiwanese population in 2005. It includes information on all medical visits and diagnoses from 2000, coded according to the International Classification of Diseases, Ninth Revision (ICD-9). From this dataset, we followed 128 651 children from birth to their fifth birthday or December 2005, whichever was earliest. All outpatient and emergency visits with a primary diagnosis of acute respiratory infection (ICD-9 460–466), acute intestinal infection (001–009), and herpangina and hand, foot, and mouth disease (HFMD) (074.0, 074.3) were identified, and the incidences of these three infectious diagnoses were estimated for each year-month throughout the follow-up period (January 2000 to December 2005). Only the first visit in each month was counted. All incidence estimates were adjusted for sex, age, or region, as appropriate, to the distribution as of January 2002. For all analyses we compared three broad geographic regions along the west coast: northern (from Keelung to Miaoli), central (Taichung, Changhua, and Nantou), and southern (from Yunlin to Pingtung) Taiwan.

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Table 1
Monthly incidence estimates of three childhood infectious diagnoses^a

| | All | By sex | | By age | | By region | | | |
|--|------------------|------------------|------------------|------------------|------------------|------------------|-----------------|------------------|--------------------|
| | | Boys | Girls | Year 0–1 | Year 2–4 | Northern | Central | Southern | Other ^b |
| Number of people at risk, mean (SD) ^c | 59 404 (4816) | 31 045 (2490) | 28 359 (2326) | 22 065 (2437) | 37 338 (2500) | 30 702 (2827) | 10 909 (702) | 15 487 (1232) | 2305 (61) |
| Monthly incidence per 1000, mean (SD) ^c | | | | | | | | | |
| <i>Acute respiratory infections</i> | | | | | | | | | |
| All year | 552 (155) | 563 (155) | 539 (154) | 532 (149) | 564 (156) | 448 (61) | 671 (88) | 650 (83) | 718 (166) |
| Spring–summer (April to September) | 515 (145) | 527 (143) | 502 (145) | 500 (145) | 525 (142) | 421 (59) | 625 (79) | 604 (73) | 672 (158) |
| Autumn–winter (October to March) | 588 (153) | 600 (155) | 575 (150) | 565 (143) | 603 (154) | 476 (50) | 717 (71) | 697 (66) | 764 (158) |
| <i>Acute intestinal infections</i> | | | | | | | | | |
| All year | 20 (21) | 21 (22) | 18 (20) | 27 (23) | 15 (17) | 14 (6) | 22 (10) | 28 (11) | 30 (30) |
| Spring–summer (April to September) | 18 (21) | 19 (22) | 17 (20) | 26 (24) | 13 (15) | 14 (6) | 20 (9) | 25 (11) | 27 (30) |
| Autumn–winter (October to March) | 22 (21) | 23 (23) | 20 (20) | 28 (23) | 17 (19) | 15 (5) | 25 (9) | 31 (11) | 33 (30) |
| <i>Herpangina and HFMD</i> | | | | | | | | | |
| All year | 14 (24) | 15 (23) | 14 (25) | 16 (26) | 13 (22) | 11 (9) | 19 (16) | 17 (13) | 22 (33) |
| Spring–summer (April to September) | 19 (29) | 20 (27) | 19 (30) | 21 (32) | 18 (26) | 15 (9) | 27 (17) | 22 (14) | 30 (40) |
| Autumn–winter (October to March) | 9 (14) | 9 (14) | 9 (15) | 10 (15) | 9 (14) | 7 (6) | 10 (10) | 11 (10) | 15 (19) |

HFMD, hand, foot, and mouth disease.

^a Incidence adjusted to the distribution by sex, age, and region in January 2002, as appropriate.

^b Other regions included Eastern Taiwan and offshore islands. Due to the small sample size this was excluded from the analyses.

^c Mean and standard deviation (SD) across 72 year-months between January 2000 and December 2005.

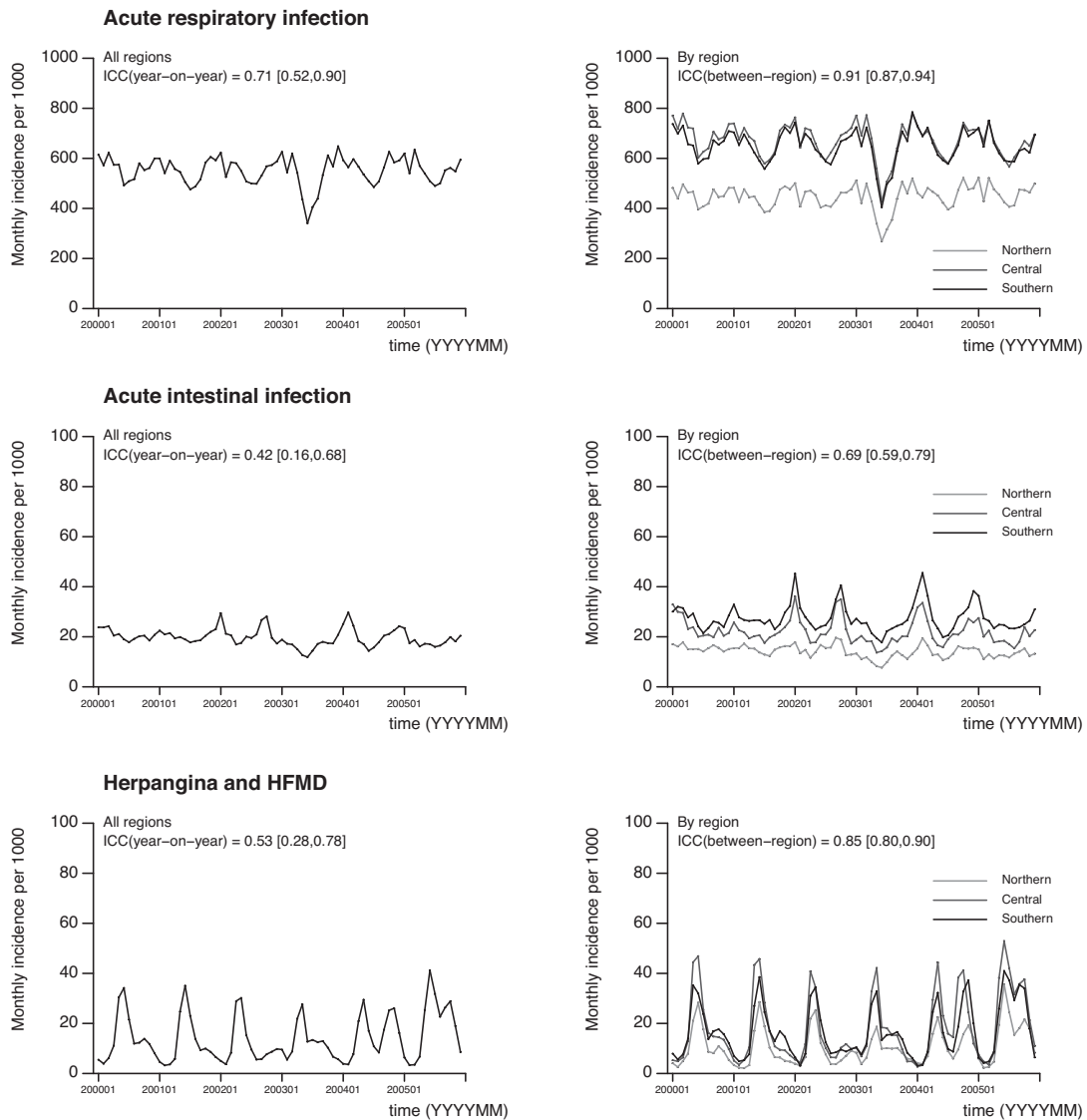


Figure 1. Monthly incidences of common childhood infections. Data based on 128 651 children aged 0–4 years in 2000–2005 selected randomly from the Taiwanese population. Diagnoses were based on the primary diagnosis according to the International Classification of Diseases, Ninth Revision. Monthly incidences were adjusted by age, sex, and region, as appropriate. Year-on-year intra-class correlations indicate annual cyclic patterns or seasonality. Between-region intra-class correlations indicate seasonal synchrony between regions. (ICC, intra-class correlations and 95% confidence intervals; HFMD, hand, foot, and mouth disease.).

As indicators of an annual cyclic pattern, i.e., seasonality, we used intra-class correlations (ICCs) to describe year-on-year consistency in monthly incidences by introducing month of the year as a random-effect term and year as a fixed-effect term in a multilevel mixed-effect linear regression model using STATA 13.0 (command *mixed* and *estat icc*). To estimate between-region seasonal synchrony in diseases with different patterns of seasonal trends, ICCs were also used to describe between-region consistency in incidence estimates across all year-month strata by introducing year-month as a random-effect term and region as a fixed-effect term.

3. Results

The average monthly incidences of the three infectious diagnoses varied with sex, age, and region (Table 1). Monthly incidences also varied with season. Incidences of acute respiratory infection and acute intestinal infection were higher during the autumn–winter seasons (October to March), and incidences of herpangina and HFMD were higher during spring–summer seasons (April to September).

We plotted the monthly incidences of these diagnoses over time (Figure 1, left column). After adjustment for age, sex, and region, we found evidence of seasonality, especially in monthly incidence for acute respiratory infection (year-on-year ICC 0.71, 95% confidence interval (CI) 0.52–0.90), and to a lesser degree for acute intestinal infection (year-on-year ICC 0.53, 95% CI 0.28–0.78) and for herpangina and HFMD (year-on-year ICC 0.42, 95% CI 0.16–0.68). An indentation was seen in almost all diagnoses in 2003, reflecting the outbreak of the severe acute respiratory syndrome, during which major quarantine was operated.⁴ Excluding this period had little effect on the intra-class correlations (data not shown). A lower baseline incidence was observed in northern Taiwan compared to central and southern Taiwan for all three types of infection (Figure 1, right column). Despite the difference in baseline incidences, we observed remarkable seasonal synchrony among the three regions, with between-region ICCs highest for acute respiratory infection (0.91, 95% CI 0.87–0.94), followed by herpangina and HFMD (0.85, 95% CI 0.80–0.90) and acute intestinal infection (0.69, 95% CI 0.59–0.79). As sensitivity analyses, we also calculated the ICCs by restricting the incidence data to either autumn–winter seasons or spring–summer seasons, and by excluding the incidence data in 2003, and the results were not substantially changed (data not shown).

4. Discussion

With a large sample size and random sampling from the entire population, we were able to record monthly variations in

incidence estimates with sufficient reliability such that the monthly details of inter-regional seasonal synchrony could be observed. Seasonal synchrony was estimated in this report within each year-month strata so that it could be applicable for diseases with different seasonal patterns. However, its interpretation could be limited by several factors. Our incidence estimates were based on medical diagnoses, which could be affected by heterogeneity in underlying aetiologies.⁵ Incidence estimates could also be affected by factors related to the tendency to seek health services when children are ill, such as cultural, socioeconomic, or medical accessibility factors, which may partly explain the differences in incidence estimates by age, sex, and region. Finally, the synchrony indicator does not differentiate among underlying causes of seasonal synchrony between regions, such as climate^{3,6} or human mobility.^{1,2} Nevertheless, in this report we introduced an indicator that could be used to describe inter-regional synchrony of infectious diseases regardless of the patterns of seasonal trend, and found strong evidence of synchrony in monthly incidence estimates for three infectious diagnoses among young children. Information on seasonal synchrony of infectious diagnoses among young children in neighbouring regions may aid in coordinating efforts in infection control measures.

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Ethics approval: This study used anonymized data. Ethics approval was not required.

Conflict of interest: We declare no conflict of interest.

References

1. Tan Y, Lam TT, Wu C, Lee SS, Viboud C, Zhang R, et al. Increasing similarity in the dynamics of influenza in two adjacent subtropical Chinese cities, following the relaxation of border restrictions. *J Gen Virol* 2014;**95**(Pt 3). <http://dx.doi.org/10.1099/vir.0.059998-0>. Epub 2013 Dec 5.
2. Viboud C, Bjornstad ON, Smith DL, Simonsen L, Miller MA, Grenfell BT. Synchrony, waves, and spatial hierarchies in the spread of influenza. *Science* 2006;**312**:447–51.
3. Xing W, Liao Q, Viboud C, Zhang J, Sun J, Wu JT, et al. Hand, foot, and mouth disease in China, 2008–12: an epidemiological study. *Lancet Infect Dis* 2014;**14**:308–18.
4. Taiwan SARS Prevention Task Force. Use of quarantine to prevent transmission of severe acute respiratory syndrome—Taiwan, 2003. *MMWR Morb Mortal Wkly Rep* 2003;**52**:680–3.
5. Bollaerts K, Antoine J, Van Casteren V, Ducoffre G, Hens N, Quoilin S. Contribution of respiratory pathogens to influenza-like illness consultations. *Epidemiol Infect* 2013;**141**:2196–204.
6. Bloom-Feshbach K, Alonso WJ, Charu V, Tamerius J, Simonsen L, Miller MA, et al. Latitudinal variations in seasonal activity of influenza and respiratory syncytial virus (RSV): a global comparative review. *PLoS One* 2013;**8**(2). <http://dx.doi.org/10.1371/journal.pone.0054445>. Epub 2013 Feb 14.