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大氣中真菌孢子與氣喘急診之相關性

Association Between Ambient Fungal Spore Concentrations and Emergency Asthma Visits

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中文摘要

研究背景：據文獻指出，2010 年約有三億人口受氣喘影響。先前的研究顯示暴露高濃度生物氣膠，與過敏、肺功能下降及其他不良之健康影響有關。生物氣膠包含花粉、真菌孢子及動、植物所產生的細胞碎片。而本篇研究主要想了解不同年齡層其氣喘發作之季節性，及真菌孢子與氣喘發作之相關性。

研究方法：空氣採樣使用 Burkard-7-day 於古亭國小三層樓高之屋頂處（同環保署空氣品質監測站地點），以 10 公升/分鐘之流速不間斷採樣，採樣時間自 2015 年 1 月至 12 月，以 1000 倍之光學顯微鏡鏡檢分析包含 26 種真菌種類，取得每日大氣真菌平均濃度 (spores/ m^3)。病例資料取自台大醫學院附設醫院 2015 年全年之急診資料，依據患者主診斷之 ICD 碼 493 判斷患者是否罹患氣喘。本研究為一病例交叉研究 (case-crossover study)，以病患自己做為其對照組，在病例確診後，同一確診月分內其他星期數則為對照組。利用條件式邏輯斯迴歸評估大氣中真菌孢子濃度與氣喘之相關性。本研究亦考慮遲滯效應(1-day lag)。

結果：研究期間共採集 309 個空氣樣本，其中以 Ascospores, *Aspergillus/Penicillium*, Basidiospores 和 *Cladosoprium* 最常見。研究期間中氣喘急診之人次達 640 次，其中又以學齡前兒童（0-5 歲兒童）之人次最多。本研究主要發現於成人中（15 歲以上），*Aspergillus/ Penicillium* 濃度會顯著提高隔日因氣喘急診之風險 (OR: 2.007, 95% CI:1.034, 3.894)，且存在劑量效應關係(p-value = 0.034)。

結論：本研究發現不同年齡層氣喘發作之季節性不同。*Aspergillus/ Penicillium* 顯著增加成人氣喘發作之風險。

關鍵字：戶外、真菌孢子、急診、氣喘、病例交叉研究

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Abstract

Background and Aim: It was estimated that about 334 million people were influenced by asthma in the world in 2010. Previous studies showed that exposing to high level of bioaerosols is associated with allergies, lung function decreasing and other adverse health effect. Bioaerosols are composed of pollens, fungal spores and debris generated by animals and plants. In this study, we aim to understand the seasonal pattern of emergency asthma visits among different age people and determine whether exposure to ambient fungal spores is associated with emergency room visit due to asthma.

Methods: The air samples were collected by Burkard 7-day recording volumetric spore trap daily on the 3-floor rooftop in Guting elementary school with 10 liters per minute of flow rate from January to December 2015. Fungal spores were identified as 26 categories by trained mycologists with 1000X microscope to retrieve the average of daily fungal spore concentrations. The health data was attained from National Taiwan University Hospital. Visits related to asthma in emergency rooms were identified by the main diagnose of ICD-9 code 493. This was a case-crossover study. The subjects were matched to themselves. After the cases were identified, we chose the control group by choosing the same day of the week in the same month. Conditional logistic regression

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was applied to examine the association between ambient fungal spore concentrations and asthma. And the 1-day lag effect was considered.

Results: There were 309 air samples in total. The most prevalent fungal spores were Ascospores, *Aspergillus/Penicillium*, Basidiospores, and *Cladosoprium*. There were 640 asthma emergency visits in National Taiwan University Hospital in 2015. The visits were contributed to children more than to adults. We found that at 1-day lag, the concentration of *Aspergillus/ Penicillium* was associated with the emergency visits due to asthma for adults (4th quartile OR: 2.007, 95 % CI: 1.034, 3.894). And there was a dose-response relationship (p-value = 0.034).

Conclusion: The seasonal pattern of emergency visits for asthma varied among different age groups. Ambient levels of *Aspergillus/ Penicillium* spores were significantly associated with asthma attack in adults with one day lag.

Keywords: Outdoor, Fungal spores, Emergency visits, Asthma, Case-crossover study

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Table of Contents

doi:10.6342/NTU201602867

List of Tables

doi:10.6342/NTU201602867

List of Figures

doi:10.6342/NTU201602867

Chapter 1 Introduction

1.1 Background

Asthma is a chronic airway disease that is characterized by recurring symptoms of airway obstruction, bronchial hyperresponsiveness and inflammation [1]. It is estimated that there were 334 million people having asthma in the worldwide dated to 2010 [2].

Asthma attacks could be triggered by colds, exercise and inhaled allergens including animal fur, dust mites, pollens and mold [2]. Previous studies have showed that exposing to high level of fungal spores is associated with allergies, lung function decreasing and other adverse health effect [3-5]. There are millions of fungi species in fungi kingdom. Locating in subtropics, Taiwan is hot and humid which make fungi easily grow and the fungal spore concentrations, in turn, are high.

A few studies have been conducted to access the ambient fungal spore concentrations in Taiwan, including in Hualien, Tainan and Greater Taipei Area (Taipei City and New Taipei City) [6-8]. But none of them has monitored the concentration daily within a whole year.

Seasonal variation has been proved to be associated with the asthma hospitalization among different areas in the world [9-11]. Since the fungal spore concentrations are affected by the meteorological factors as well, there lays the importance of evaluating

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the relation between fungal spore concentrations and asthma attack in specific region.

1.2 Objectives

It led to two objectives in this study:

1. To elucidate the seasonal pattern of asthma in emergency visits and the fungal spore concentrations.
2. To determine whether ambient fungal spore concentrations is associated with asthma.

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Chapter 2 Literature Review

Asthma prevalence is increasing and remains high in many regions. In the United States, asthma prevalence has increased from 7.3% in 2001 to 8.4% in 2010 [12]. According to a national study in Taiwan, asthma caused 1.1% of total hospital admissions in 2000 [13]. And another study reported that the asthma prevalence was 11.9% in 2007 [14]. Asthma caused by well-recognized fungi, such as *Alternaria alternate,* are often mediated in Type I immunoglobulin (Ig) E / TH_2 hypersensitivity [15, 16].

A population-based study was done in Taiwan during 1998-2001 and implied the fact that hospitalization peak for adult asthma was between January and March [13]. However, among 0-4 years old children, there was a peak in November and a trough in February. Fleming, et al., have also proposed that the seasonal pattern of asthma evolved with age [9].

As far as the fungal spores are concerned, airborne fungal spores fall in 2-10 μm, which is able to penetrate the lower bronchi and leads to the allergies of lower respiratory tract, for example, asthma. [16, 17]. The average concentration of total fungal spores was 4844.41 spores/m^3 in Hualien [6], the eastern coast of Taiwan, and

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2564.98 spores/m^3 in the Greater Taipei area (Taipei City and New Taipei City), the northern of Taiwan [8]. It is reported that high temperature (15-29°C), high relative humidity (50–80%) and rainfall are the necessities of fungal spores formation of *Alternaria* and *Cladosporium* [18], which were proved that sensitization to these fungal spores would be the risk factors for severe asthma in adults in Europe [19].

With the respect to epidemiological evidence, in London, when 0-14 years old children exposed to the high concentration of ambient fungal spores (the interquartile range of total fungal spores concentrations = 3311.6 spores/m^3), the risk of paying emergency visits and hospital admissions due to asthma increased even though it was insignificant [20]. Another study conducted in Ottawa found out the emergency visits due to asthma in a regional hospital were associated with *Deuteromycetes, Basidiomycetes* and *Ascomycetes*, which the average of spores concentrations were 1672 spores/m^3, 551 spores/m^3 and 297 spores/m^3 in order [21].

From the literature reviewed above, there is no consistent fungal taxon associated to the emergency visits for asthma. Even though the seasonal pattern of emergency admissions for asthma has been investigated before, the yearly information of fungal spore concentrations is lack. Although many studies have inspected the effect of

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metrological factors on fungal spores, it would be nice to have the bigger picture of the fungal spore concentrations and the related health effect.

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Chapter 3 Materials and Methods

3.1 Study Design

This was a time stratified case-crossover study to evaluate the effect of ambient fungal spore concentrations on emergency visits of asthma. This study recorded daily ambient fungal spore concentrations, which were assumed to be the personal exposure, from January to December 2015. The study population was those patients who paid emergency visits due to asthma in a regional hospital, National Taiwan University Hospital, in Taipei, Taiwan.

3.2 Air Samples

Fungal spores were collected by Burkard 7-day recording volumetric spore trap (Burkard Manufacturing Co. Limited, Rickmansworth Hertfordshire, England) and sampled 24 hours continuously with 10 liters per minute. The flow rate was calibrated once a week while the drum was changed. The sampling protocol referred to Pan-American Aerobiology Association (PAAA) was as follows: A thin layer of Lubriseal grease (Thomas Scientific, Swedesboro, NJ) was coated onto the Melinex tape which mounted the drum. The rotating frequency of the drum was 2 mm per hour. The particles, including aerosols and bioaerosols, impacted on the Melinex tape through a 2mm X 14 mm inlet. After sampling, the Melinex tape was cut into 7 pieces with 48

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mm in length of each, adhered to the slide by 10% Moviol and in turn stained by Glycerin Jelly before identification. One single longitudinal traverse near the middle of the trace was identified under the 1000 X microscope. Fungal categories were the same as those decided by American Academy of Allergy Asthma & Immunology (AAAAI). There were 26 categories including other and unidentified. The observed fungal spores number could be converted into the concentration (spores/m^3) by equation (1) and (2).

$$Average\ \ Daily\ \ Concentration\ \ \left(\frac{spores}{m^3}\right) = \frac{Number\ \ of\ \ spores\ \ (spores\,)}{Volume\ \ (m^3)} \quad \text{equation(1)}$$

$$Volume\ \ (m^3) = \frac{Field\ \ Diameter\ \ of\ \ Objective\ \ (mm)}{Trace\ \ Width(mm)} \times Flow\ \ Rate \times\ \ Time \quad \text{equation(2)}$$

where, the field diameter of objective was 0.25 mm, trace width was 14 mm, flow rate was 0.01m^3/ min, and time was 1440 minutes.

The sampler was placed on the 3-floor rooftop in Guting Elementary School (longitude: 121.53°, latitude: 25.02°) in Taipei City right next to the air monitoring station founded by Environmental Protection Administration. The sampling period was from January to December 2015. There were some missing dates of sampling including New Year vacation (1/1-1/7), Chinese New Year vacation (2/12-2/25), failure of drum exchange (8/13-8/26) and power-supplied problem (10/1-10/21).

3.3 Data of Health Outcome

doi:10.6342/NTU201602867

The health data was retrieved from National Taiwan University Hospital (NTUH) during January to December 2015. The enrollees were those who paid the visit to emergency department due to the asthma. NTUH is about 2.5 km away from the air-sampling site, a tertiary referral center with 2400s beds. Daily emergency visits were recorded by identifying the main diagnose of ICD-9 (International Classification of Diseases, Ninth Revision) code 493. This study was approved by the Institutional Review Board of the Ethics Committee of the NTUH.

3.4 Data of Meteorological Factors

We have retrieved the meteorological factors during the studying period from the open source of Taiwan Environmental Protection Administration in Guting air monitoring station. We obtained the hourly data and calculated for the daily data by applying arithmetic mean. The meteorological factors include the temperature, relative humidity and concentration of CO (by non-dispersive infrared), NO_2 (chemiluminescence), SO_2 (by ultraviolet fluorescence), O_3 (by ultraviolet absorption), PM_{10} (by beta-ray attenuation), and $PM_{2.5}$ (by beta-ray attenuation).

3.5 Statistical Analysis

The software to perform the data analysis was Microsoft Excel, JMP 10 and SAS

doi:10.6342/NTU201602867

ver9.3 (SAS Institute Inc., Cary, NC, USA). The characteristics of the fungal spore concentrations distribution and the characteristics of the asthma patients were presented by the descriptive statistics. Conditional logistic regression was applied to examine the ambient fungal spore concentration and emergency visits of asthma and the seasonal impact. And we tested the dose-response relationship as well. The association between meteorological factors and emergency asthma visits was assessed in order to adjust the model. The analysis included 0-day lag effect, which meant that the exposure of the subjects was the same day as the asthma attacked, and 1-day lag effect, which meant that the exposure of the subjects was a day before the asthma attacked. We transferred the fungal spore concentrations into ordinal variables due to that some fungal spore concentrations were relatively low. In order to reflect the exposure reality, we discarded the point estimate per log 10 increase of fungal spore concentrations.

There were three approaches to make the concentration of fungal spores into ordinal variables. First, we would examine the median of fungal spore concentrations. When the median concentration was zero, we would consider whether the specific fungal spores were presented in the sampling day or not in our analysis. Another criterion would focus on the fungal spore concentrations at 25 % percentile. When it was zero, the exposure

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level would be cut into three groups: zero concentration, lower than the median concentration of specific fungal spores and higher than the median concentration. The remains would be categorized into quartiles by referring to the concentration of 25%, 50%, and 75% percentile.

In this study, we used time stratified case-crossover study due to the exposure varying in short term and an abrupt health outcome [22]. The study design controls the confounding factors of the individuals to remain constant in hazard period and control period by matching the subjects to themselves [23]. After the cases were indicated, they were matched by selecting the same day of the week in the same month as the control period, which could be 7 to 28 days before or later at a week interval, and it led to 3 to 4 control periods per case.

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Chapter 4 Results

4.1 Fungal Spores

There were 309 air-sampling samples in total. Table 1 showed the distribution of fungal spore concentrations during the study period. The table was ordered by the frequency; however, high frequency was not required to be in high concentration. The highest fungal spore concentrations were Ascospores, *Aspergillus /Penicillium,* Basidiospores, *Cladosporium,* which were 1850.47 spores/m^3, 372.62 spores/m^3, 1500.68 spores/m^3, and 521.19 spores/m^3. In the meanwhile, these were also the most prevalent fungal categories as well.

Figure 1 showed the temporal differences of the monthly average of the most prevalent spore concentrations in 2015. Whichever the fungal spore was, the highest concentration was in July. For *Cladosporium*, the variation within the whole year was relatively small, compared to other fungal categories. As to *Aspergillus/ Penicillium*, the concentration was relatively low; however, the temporal trend was same as total spore concentrations.

4.2 Health Outcome

There were 640 emergency visits due to asthma in NTUH in 2015. The descriptive

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statistics was shown in Table 2. According to the age of the patients, the visits were divided into three subgroups, 0-5 (including 5) years old, 5-15 (including 15) years old, and elder than 15 years old. Preschool children (0-5 years old) paid the most visits during the study period. In spite of the age, there was a little difference between the genders. 372 visits were contributed to female and 268 to male. And the average of daily emergency asthma visits were 1.75 visits /day.

The temporal distributions of monthly average of total fungal spore concentrations and emergency visits related to asthma were plotted in figure 2. There was only a peak, which was between June and July, of high concentration of total spores. On the contrary, the emergency visits, in generally, was high between March and May and followed by a decrease and a trough in July, and then the trend inclined in September to reach the peak in December.

Figure 3 showed the overall emergency asthma visits and also interpreted in terms of different age subgroups in each month in 2015. Preschool children intended to suffer from asthma in fall and early winter (October, November, and December). School-aged children (from 5 to 15 years old) paid more visits in May and September. In addition, there were two clearly trough in August and January. To adults, elder than 15 years old,

doi:10.6342/NTU201602867

the variation was mild, but, generally, the visits were more in winter.

4.3 Association between Fungal Spores and Asthma

The individual fungal spore concentrations were evaluated in the conditional logistic regression model one after another and correlated with the subjects in different age groups. The result of 0-day lag was presented in Table 3. *Cercospora, Drechslera/ Helminthosporium, Epicoccum, Oidium/Erysiphe, Peronospora, Pithomyces*, Rusts, *Stemphylium, Tetrapola, Ulocladium,* which had low frequency (<20%) were not analyzed in the model.

We did not find the association between meteorological factors and emergency visits of asthma (the data was not shown). Thus, there was no additional adjustment in our model to evaluate the correlation of fungal spore concentrations and emergency asthma visits. At 0-day lag, *Curvularia* was inversely related to children under 5 years old (concentration higher than median OR: 0.605, 95%CI: 0.402 - 0.911); however, as to adults elder than 15 years old, *Curvularia* had significantly increased the odds ratio of emergency visits related to asthma (concentration higher than median OR: 1.664, 95% CI: 1.071 – 2.587).

The effect of 1-day-lag was shown in Table 4. We found that *Arthrinium* was related

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to children under 5 years old (second quartile OR: 0.525, 95% CI: 0.329 – 0.839). *Curvularia,* on the other hand, was correlated to school-aged children (concentration higher than median OR: 0.517, 95% CI: 0.310 – 0.861). And we found the association between *Aspergillus/ Penicillium* and emergency asthma visits in adults (forth quartile OR: 2.007, 95% CI: 1.034 – 3.894).

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Chapter 5 Discussion

5.1 Fungal Spores

In this study, we have successfully monitored the fungal spore concentrations within a whole year, except for some inevitable episodes. The average of total fungal spores concentration was 4448.08 spores/m^3 in our study, which was far lower than that in Tainan [7]. Possibly because the weather condition in southern Taiwan, the tropical area, was more appropriate for fungi growing. However, we share the common prevalent fungal spore categories with other studies [6-8].

In our study, we found that Ascospores, *Aspergillus /Penicillium,* Basidiosporess, *Cladosporium,* Smuts, *Arthrinium, Nigrospora* and *Periconia* presented more than 60 % in our air samples. It is reported that Ascospores, *Cladosporium, Aspergillus/Penicillium, Ganoderma* (belongs to *Basidiomycetes*), *Arthrinium/Papularia* were the major fungal categories in Hualien [6]. In Tainan, the predominant fungal categories were *Cladosporium,* Ascospores, *Periconia,* Basidiospores, *Botrytis,* Smuts, *Alternaria, Penicillium/ Aspergillus, and Fusarium* [7]. Last but not least, the study conducted in Greater Taipei Area found the leading fungal categories were Ascospores, *Aspergillus/ Penicillium,* Basidiospores, *Cladosporium,*

doi:10.6342/NTU201602867

Smuts*, Fusarium, Periconia, Nigrospora, Botrytis,* and *Arthrinium* [8]. In addition, in our study, we found that most of fungal spores were in high concentration in summer (June, July and August), and low concentration in winter (December, January and February).

5.2 Health Outcome

March and December were two periods having more emergency visits related to asthma in NTUH in 2015. The result was similar to another study, which extracted the subjects from National Health Insurance Research Database (NHIRD), in Taipei City from 2000 to 2002 [24]. NHIRD, which covered more than 96% of the population in 2000, was the database provided by the Bureau of NHI [25].

We indicated the seasonal variation of the emergency asthma visits among different age groups. From table 2, most of the visits were contributed to children (both preschool children and school-aged children) than to adults. There are some possible explanations.

Firstly, compared to adults, children are engaged in more outdoor activities, hence it increased the exposure of ambient fungal spores [26]. Secondly, the process of lung development is significant in childhood and the alveoli numbers in lungs continue

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changing through adolescence. This suggested that the incomplete development of lung might lead to certain level of damage from given exposure of fungal spore concentrations [26, 27]. As the characteristics of asthma, chronic illness and recurring symptoms, adults patients are likely to have more experience dealing to the disease when the asthma attacks. They may have self-treat for mild asthma or pay the visits to nearby clinics instead of visiting emergency rooms. On the contrary, whenever the children have asthma attack, parents rush to bring the children to the hospitals [24, 26].

We speculated that the high number of visits among all age groups might result from the flu and low temperature other than fungal spores exposure, especially for the preschool children, who had poor immunity [28]. The temporal trend of paying emergency asthma visits in school-aged children interestingly coincided with the schooling time. In Taiwan, there's a summer vacation in July and August and a winter vacation along with Chinese New Year holiday in mid-January and February. The emergency asthma visits dramatically dropped during these periods and increased thereafter. The phenomenon also occurred in New Zealand, Malta, Sydney, and the UK [10, 11, 29, 30]. It was probably because of that children increased social contacts in schools and in turn increased the risks of suffering from viral infections in respiratory

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tracts [11, 29].

5.3 Association Between Fungal Spores and Asthma

Many current studies divided fungal categories into three main phyla: *Ascomycota, Basidiomycota* and *Deuteromycota*. In our study, we examined the fungal categories down to the taxon, except for some categories that were not easily to tell the apart from the morphology. We found that the concentration of *Aspergillus/ Penicillium* was positively associated with emergency asthma visits to adults at 1-day lag. Besides, from the trend test, we could tell that there's a dose-response relationship. In southern Pakistan, they found that the higher indoor concentration of *Aspergillus/ Penicillium* was correlated to higher adults (≥16 years old) asthma exacerbation [31]. Dales et al., has indicated that *Deutermycetes* (including *Aspergillus/ Penicillium*) increased 1.9% of the emergency visits for asthma in a regional children hospital study [21]. Another study in Taiwan also revealed that the classroom concentration of *Aspergillus/ Penicillium* was related to current asthma in school-aged children [3].

Curvularia played as different roles among different age groups from our findings. To preschool children and school-aged children, *Curvularia* was inversely correlated to emergency visits due to asthma at 0-day-lag and 1-day-lag respectively. On the other

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hand, to adults, the positive relation between *Curvularia* and emergency asthma visits was found. The evidence and the mechanism of *Curvularia* and asthma were limited and unclear. However, the relationship between *Curvularia* and other respiratory disease did exist. In 1981, McAleer et al., shared a case report of a 33 year-old woman having allergic bronchopulmonary disease caused by *Curvularia lunata* [32]. And from the previous literature, *Curvularia* was one of the common fungi in allergic bronchopulmonary mycosis (ABPM). Other than *Aspergillus*, the prevalence of the cases was 8% [33].

At 1-day lag, the 2^{nd} quartile concentration of *Arthrinium* was found to be negatively associated with emergency visits due to asthma. Nevertheless, the trend test did not meet statistically significance.

To sum up, from our study results, we did not find the association between emergency asthma visits and prevalent fungal spores but *Aspergillus/ Penicillium*. Previous study suggested that 1500 spores/ m^3 of *Cladosporium* was the threshold of decreasing the lung function for school children [4]. This might explain the insignificant result of *Cladosporium* in our study. The average concentration of *Cladosporium* from what we observed was 529.19 spores/m^3, which was far lower than the threshold. The

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results might not be applied to other regions due to the spatial variation of fungal spores. We did not either encourage exposing more of those fungal spores playing a protective factor in our study. Here, only acute asthma was examined. There might be some other adverse health effects of exposing high level of fungal spores, such as allergic bronchopulmonary mycosis (ABPM) [33]. What's more, the exposure of fungal spores was a mixture exposure along with particles, pollens and other air pollutants. Therefore, the interactions between fungal spores itself and other pollutants might be the next target to work on. In this case, the policy makers would have the insight to set a threshold for warning the public before engaging in outdoor activities.

5.4 Strengths and Limitations

To our knowledge, this was one of the few study that continuously monitoring the temporal variation of fungal spore concentrations almost a year in Taipei. Having the complete data, we could better understand the different trends between fungal spore concentrations and the asthma. Even Taiwan is a small island with approximately 36,000 km^2, the spatial variation of fungal spore concentrations still remains. Additionally, this was a case-crossover study, we controlled the personal characteristics, such as gender, environmental tobacco smoke and the effects of day of the week, which

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secondary data did not provide [22, 34].

There are limitations in this study. Since this was a hospital-based study, the case number was limited. Furthermore, we did not know the general population of how many people were at risk. In this case, the temporal trend of emergency asthma visits could only be presented in case number instead of the rate.

Another potential problem is that whether the one and only monitoring cite could represent the exposure of the individuals. In addition, because of the privacy protection, we assumed that all the subjects exposed to the fungal spores in the same region where the air sampling conducted. Due to the limited manpower, we failed to access the fungal spore concentrations in different locations. This was the difficulty that environmental epidemiology studies often encountered.

We also face multiple comparisons in the statistical analysis. This might have resulted increased chance of false positive findings. The results of association between *Aspergillus/ Penicillium* spores and emergency visit due to asthma have to be further examined.

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Chapter 6 Conclusion

This study found that Ascospores, *Aspergillus /Penicillium,* Basidiosporess, *Cladosporium,* Smuts, *Arthrinium, Nigrospora* and *Periconia* were the predominant fungal spore categories in our samples after monitoring for almost a year. Ambient level of *Aspergillus/ Penicillium* spores was positively associated with emergency visits due to asthma in adults (above 15 years old) with one day lag.

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Table 1 Distribution of fungal spore concentrations (spores/m3) in 2015

Fungal Categories	**Freq(%)**	**Mean**	**Q1**	**Median**	**Q3**	**SD**	**Min**	**Max**
Total Fungal Spores	100.00	4448.08	1244.44	2838.89	6525.56	4187.03	155.56	18950.56
Ascospores	100.00	1850.47	501.67	1170.56	2582.22	1890.24	31.11	9601.67
Aspergillus/Penicillium	100.00	372.62	97.22	221.67	521.11	432.04	11.67	4281.67
Basidiospores	99.68	1500.68	167.22	758.33	2247.78	1747.74	0.00	8458.33
Cladosporium	99.68	529.19	143.89	326.67	688.33	589.07	0.00	3780.00
Smuts	95.47	69.18	19.44	46.67	101.11	69.62	0.00	416.11
Arthrinium	77.02	18.63	3.89	11.67	23.33	29.92	0.00	272.22
Nigrospora	69.26	10.47	0.00	3.89	15.56	14.79	0.00	116.67
Periconia	63.75	7.15	0.00	3.89	11.67	9.05	0.00	50.56
Curvularia	53.40	5.69	0.00	3.89	7.78	8.85	0.00	58.33
Botrytis	53.07	17.59	0.00	3.89	23.33	32.14	0.00	194.44
Torula	51.13	6.20	0.00	3.89	7.78	9.76	0.00	77.78
Fusarium	42.72	7.27	0.00	0.00	7.78	15.77	0.00	167.22
Alternaria	39.16	3.67	0.00	0.00	3.89	7.03	0.00	54.44
Cercospora	19.74	1.69	0.00	0.00	0.00	4.69	0.00	35.00
Drechslera/Helminthosporium	11.00	0.79	0.00	0.00	0.00	3.77	0.00	50.56
Peronospora	9.71	0.94	0.00	0.00	0.00	4.47	0.00	58.33
Rusts	8.41	0.58	0.00	0.00	0.00	3.46	0.00	54.44
Pithomyces	6.80	0.33	0.00	0.00	0.00	1.33	0.00	11.67
Tetrapola	5.18	0.24	0.00	0.00	0.00	1.21	0.00	15.56
Oidium/Erysiphe	4.53	0.21	0.00	0.00	0.00	1.04	0.00	7.78
Epicoccum	3.24	0.14	0.00	0.00	0.00	0.79	0.00	7.78
Steymphylium	3.24	0.15	0.00	0.00	0.00	0.87	0.00	7.78
Ulocladium	0.32	0.01	0.00	0.00	0.00	0.22	0.00	3.89
Polythrincium	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Other Fungi	80.58	29.42	3.89	19.44	42.78	35.00	0.00	202.22
Unidentified Fungi	72.82	14.13	0.00	3.89	15.56	22.88	0.00	155.56

Freq - Frequency: The percentage of samples presented (n=309).

Q1- First Quartile, Q3 - Third Quartile, SD - Standard Deviation, Min – Minimum, Max- Maximum

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Table 2 Characteristics of the emergency visits for asthma in NTUH in 2015

Characteristics	Number of visits (%)	Mean (visits/day)
All subjects	640 (100)	1.75
Age		
≤5 years old	263 (41.1)	0.72
5-15 years old	180 (28.1)	0.49
>15 years old	197 (30.8)	0.54
Gender		
Female	268 (41.9)	0.73
Male	372 (58.1)	1.02

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Table 3 Conditional logistic regressions for fungal spore concentrations and emergency asthma visits at 0-day-lag in different age groups

Fungal Spore		≤5 years old			5-15 years old			>15 years old		
Categories		OR	95%CI	P_{trend}	OR	95%CI	P_{trend}	OR	95%CI	P_{trend}
Total spores	Q1	1.000		0.640	1.000		0.950	1.000		0.312
	Q2	0.905	0.587, 1.394		0.933	0.538, 1.618		0.987	0.595, 1.637	
	Q3	1.078	0.659, 1.763		0.888	0.472, 1.670		0.721	0.403, 1.291	
	Q4	1.091	0.623, 1.912		1.030	0.507, 2.094		0.776	0.391, 1.540	
Alternaria	No	1.000			1.000			1.000		
	Yes	1.004	0.702, 1.436		1.035	0.688, 1.558		0.847	0.563, 1.276	
Ascospores	Q1	1.000		0.739	1.000		0.577	1.000		0.079
	Q2	1.068	0.682, 1.673		1.107	0.592, 2.071		0.660	0.391, 1.113	
	Q3	0.889	0.529, 1.494		1.046	0.524, 2.089		0.561	0.308, 1.023	
	Q4	0.935	0.523, 1.670		1.249	0.604, 2.583		0.561	0.281, 1.120	
Asper/Penici	Q1	1.000		0.394	1.000		0.961	1.000		0.878
	Q2	1.001	0.641, 1.563		1.297	0.764, 2.203		0.858	0.530, 1.389	
	Q3	0.924	0.553, 1.544		0.933	0.511, 1.704		0.816	0.472, 1.411	
	Q4	1.345	0.761, 2.377		1.135	0.584, 2.206		0.998	0.547, 1.821	
Arthrinium	Q1	1.000		0.773	1.000		0.682	1.000		0.529
	Q2	0.979	0.631, 1.521		1.121	0.639, 1.969		0.889	0.534, 1.479	
	Q3	0.832	0.534, 1.294		1.496	0.937, 2.387		0.761	0.455, 1.272	
	Q4	1.155	0.765, 1.744		0.926	0.550, 1.557		0.908	0.555, 1.486	
Basidiospores	Q1	1.000		0.776	1.000		0.121	1.000		0.286
	Q2	0.955	0.578, 1.577		1.312	0.664, 2.592		1.049	0.581, 1.895	
	Q3	1.008	0.589, 1.726		1.629	0.768, 3.455		0.809	0.420, 1.559	
	Q4	0.885	0.477, 1.641		1.847	0.803, 4.251		0.775	0.363, 1.626	
Botrytis	0	1.000		0.960	1.000		0.590	1.000		0.497
	≤M	0.868	0.513, 1.466		0.907	0.490, 1.680		0.890	0.452, 1.752	
	>M	1.027	0.669, 1.575		1.154	0.705, 1.889		1.196	0.718, 1.992	
Cladosporium	Q1	1.000		0.937	1.000		0.600	1.000		0.375
	Q2	1.210	0.799, 1.830		0.606	0.357, 1.029		0.675	0.395, 1.152	
	Q3	0.910	0.584, 1.418		0.826	0.474, 1.441		1.113	0.677, 1.830	
	Q4	1.106	0.726, 1.686		1.064	0.652, 1.736		1.132	0.692, 1.851	
Curvularia	0	1.000		**0.011**	1.000		0.288	1.000		0.050

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	≤M	0.704	0.473, 1.046		1.233	0.782, 1.944		0.822	0.504, 1.342	
	>M	0.605*	0.402, 0.911		1.267	0.807, 1.987		1.664*	1.071, 2.587	
Fusarium	No	1.000			1.000			1.000		
	Yes	0.713	0.496, 1.027		1.031	0.679, 1.565		0.973	0.622, 1.522	
Nigrospora	0	1.000		0.880	1.000		0.158	1.000		0.187
	≤M	0.952	0.623, 1.455		1.173	0.675, 2.039		1.623	0.981, 2.684	
	>M	1.026	0.703, 1.497		1.398	0.869, 2.248		1.378	0.874, 2.173	
Periconia	0	1.000		0.169	1.000		0.707	1.000		0.811
	≤M	1.187	0.806, 1.750		1.072	0.666, 1.727		1.091	0.636, 1.710	
	>M	1.305	0.887, 1.920		0.912	0.582, 1.428		1.044	0.668, 1.631	
Smuts	Q1	1.000		0.846	1.000		0.924	1.000		0.222
	Q2	0.809	0.515, 1.273		1.152	0.665, 1.997		1.016	0.596, 1.732	
	Q3	0.790	0.502, 1.245		1.091	0.630, 1.888		1.136	0.676, 1.909	
	Q4	1.069	0.665, 1.717		1.061	0.586, 1.924		1.493	0.812, 2.747	
Torula	0	1.000		0.699	1.000		0.339	1.000		0.303
	≤M	0.838	0.532, 1.320		0.829	0.476, 1.442		1.277	0.784, 2.079	
	>M	0.948	0.670, 1.343		0.818	0.541, 1.237		1.215	0.807, 1.828	

p-value < 0.05 ** p-value < 0.005

Bold-faced showed statistically significant trend.

Q1-Q4: First to forth quartile.

No /0: Specific fungal spores did not present.

Yes: Specific fungal spores presented.

≤M: Fungal spore concentrations were below median.

>M: Fungal spore concentrations were above median.

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Table 4 Conditional logistic regressions for fungal spore concentrations and emergency asthma visits at 1-day-lag in different age groups

Fungal Spore		<=5			5-15			>15		
Categories		OR	95%CI	P_{trend}	OR	95%CI	P_{trend}	OR	95%CI	P_{trend}
Total spores	Q1	1.000		0.934	1.000		0.348	1.000		0.243
	Q2	0.760	0.497, 1.163		1.145	0.671, 1.954		1.173	0.692, 1.987	
	Q3	0.933	0.573, 1.519		0.876	0.475, 1.617		1.227	0.675, 2.230	
	Q4	0.939	0.536, 1.643		1.544	0.789, 3.019		1.550	0.772, 3.111	
Alternaria	No	1.000			1.000			1.000		
	Yes	1.094	0.767, 1.562		1.054	0.685, 1.620		0.949	0.635, 1.416	
Ascospores	Q1	1.000		0.744	1.000		0.975	1.000		0.301
	Q2	1.134	0.724, 1.776		0.843	0.478, 1.486		1.088	0.635, 1.862	
	Q3	1.037	0.616, 1.746		0.899	0.491, 1.646		1.151	0.603, 2.200	
	Q4	1.125	0.617, 2.053		0.992	0.528, 1.862		1.452	0.735, 2.867	
Asper/Penici	Q1	1.000		0.536	1.000		0.464	1.000		**0.034**
	Q2	0.931	0.594, 1.458		1.152	0.674, 1.969		1.033	0.619, 1.722	
	Q3	1.288	0.819, 2.024		0.856	0.469, 1.561		1.455	0.816, 2.595	
	Q4	1.025	0.592, 1.775		1.501	0.767, 2.937		2.007*	1.034, 3.894	
Arthrinium	Q1	1.000		0.871	1.000		0.772	1.000		0.342
	Q2	0.525*	0.329, 0.839		1.094	0.648, 1.847		0.753	0.448, 1.266	
	Q3	1.056	0.715, 1.560		0.658	0.380, 1.139		1.241	0.761, 2.022	
	Q4	0.870	0.569, 1.330		1.260	0.790, 2.010		1.145	0.714, 1.836	
Basidiospores	Q1	1.000		0.678	1.000		0.718	1.000		0.668
	Q2	0.902	0.548, 1.485		1.367	0.699, 2.673		1.079	0.616, 1.889	
	Q3	1.230	0.712, 2.125		0.816	0.389, 1.713		0.850	0.440, 1.641	
	Q4	0.980	0.522, 1.837		1.506	0.683, 3.320		1.297	0.637, 2.644	
Botrytis	0	1.000		0.629	1.000		0.098	1.000		0.717
	≤M	1.050	0.622, 1.774		1.469	0.764, 2.822		1.557	0.834, 2.907	
	>M	1.114	0.718, 1.727		1.542	0.925, 2.572		1.076	0.654, 1.769	
Cladosporium	Q1	1.000		0.885	1.000		0.747	1.000		0.625
	Q2	0.997	0.665, 1.492		0.886	0.533, 1.473		0.956	0.580, 1.576	
	Q3	0.858	0.549, 1.342		0.957	0.576, 1.592		0.850	0.519, 1.394	
	Q4	1.098	0.703, 1.714		1.080	0.658, 1.773		0.924	0.532, 1.604	
Curvularia	0	1.000		0.662	1.000		**0.009**	1.000		0.732

doi:10.6342/NTU201602867

	≤M	1.033	0.703, 1.518		0.660	0.416, 1.048		0.948	0.595, 1.511	
	>M	1.091	0.739, 1.612		0.517*	0.310, 0.861		0.928	0.589, 1.462	
Fusarium	No	1.000			1.000			1.000		
	Yes	1.011	0.714, 1.431		0.861	0.573, 1.294		0.910	0.578, 1.433	
Nigrospora	0	1.000		0.698	1.000		0.323	1.000		0.063
	≤M	1.116	0.725, 1.717		0.738	0.436, 1.251		1.291	0.788, 2.116	
	>M	0.933	0.637, 1.368		0.793	0.511, 1.232		1.535	0.979, 2.407	
Periconia	0	1.000		0.755	1.000		0.909	1.000		0.220
	≤M	0.751	0.506, 1.115		0.905	0.553, 1.481		1.086	0.703, 1.679	
	>M	0.971	0.666, 1.415		0.975	0.635, 1.497		0.729	0.470, 1.130	
Smuts	Q1	1.000		0.819	1.000		0.971	1.000		0.193
	Q2	1.010	0.645, 1.582		0.697	0.403, 1.205		1.003	0.582, 1.729	
	Q3	0.952	0.608, 1.490		0.613	0.348, 1.082		1.324	0.791, 2.216	
	Q4	0.961	0.563, 1.639		1.035	0.571, 1.877		1.391	0.751, 2.577	
Torula	0	1.000		0.604	1.000		0.521	1.000		0.580
	≤M	0.885	0.565, 1.387		0.854	0.487, 1.497		1.329	0.806, 2.192	
	>M	0.918	0.641, 1.316		0.875	0.575, 1.334		1.084	0.719, 1.635	

p-value < 0.05   ** p-value < 0.005

Bold-faced showed statistically significant trend.

Q1-Q4: First to forth quartile.

No /0: Specific fungal spores did not present.

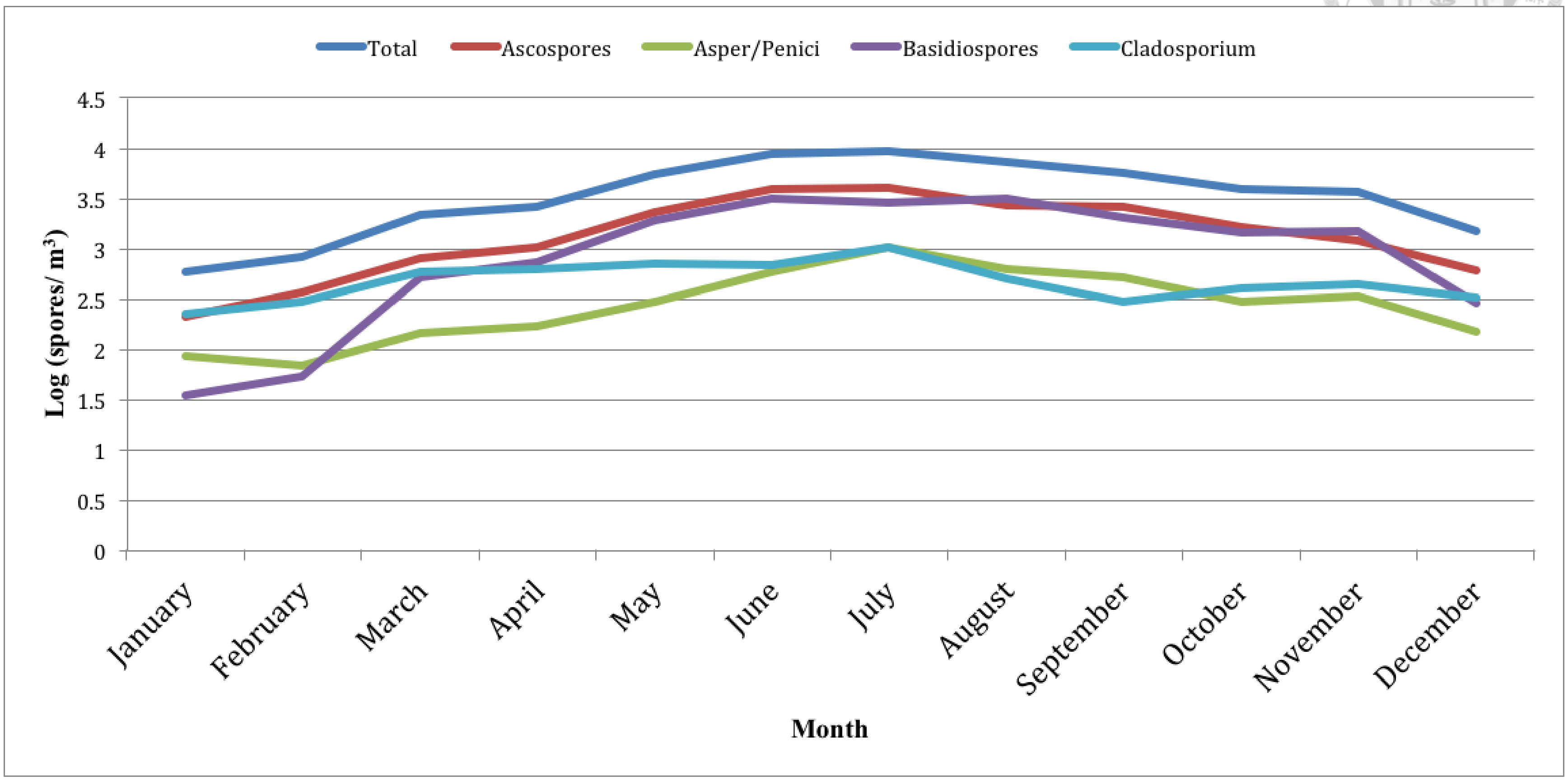
Yes: Specific fungal spores presented.

≤M: Fungal spore concentrations were below median.

>M: Fungal spore concentrations were above median.

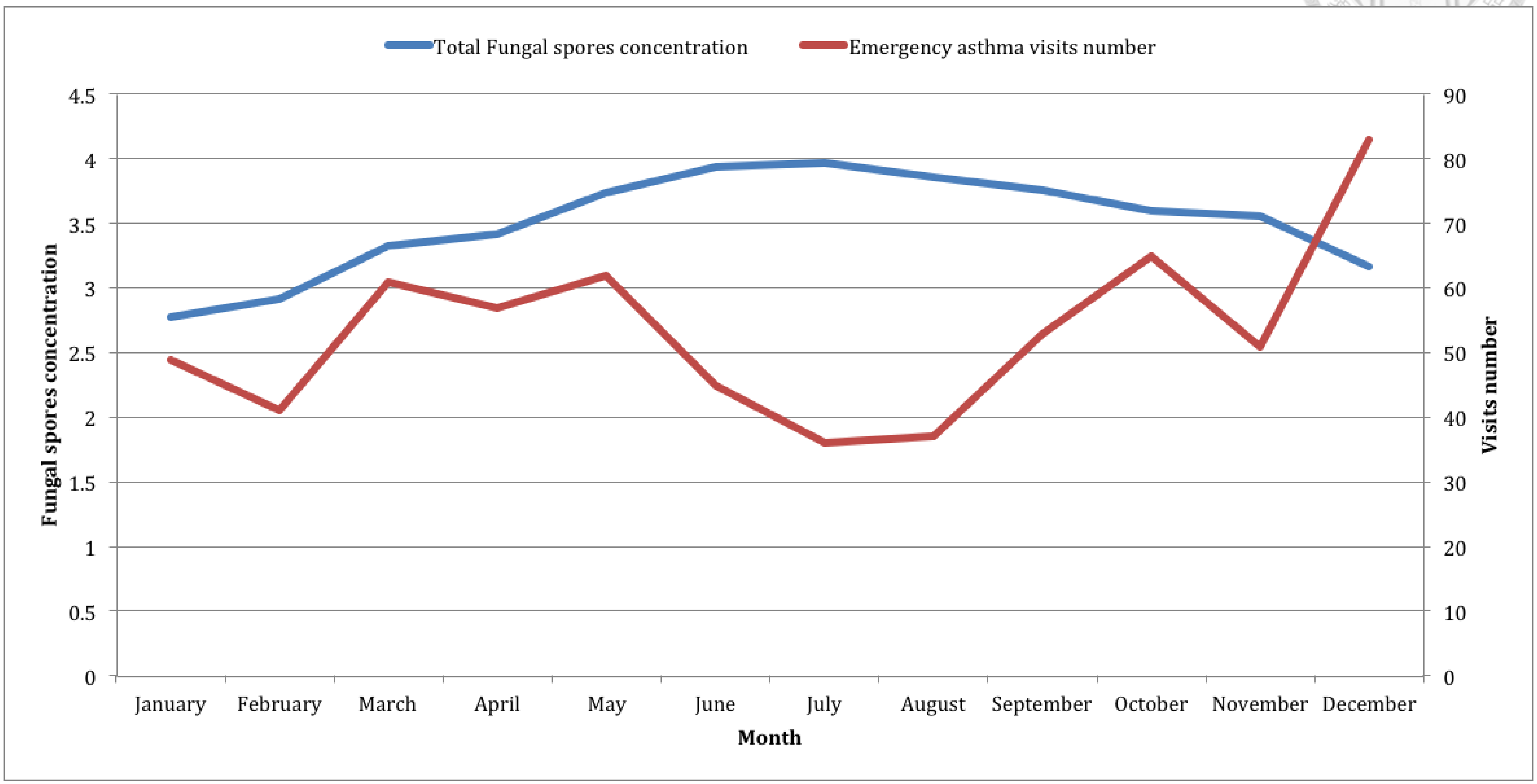
doi:10.6342/NTU201602867

Figure 1 Temporal trend of the most prevalent fungal spores monthly average concentrations in 2015



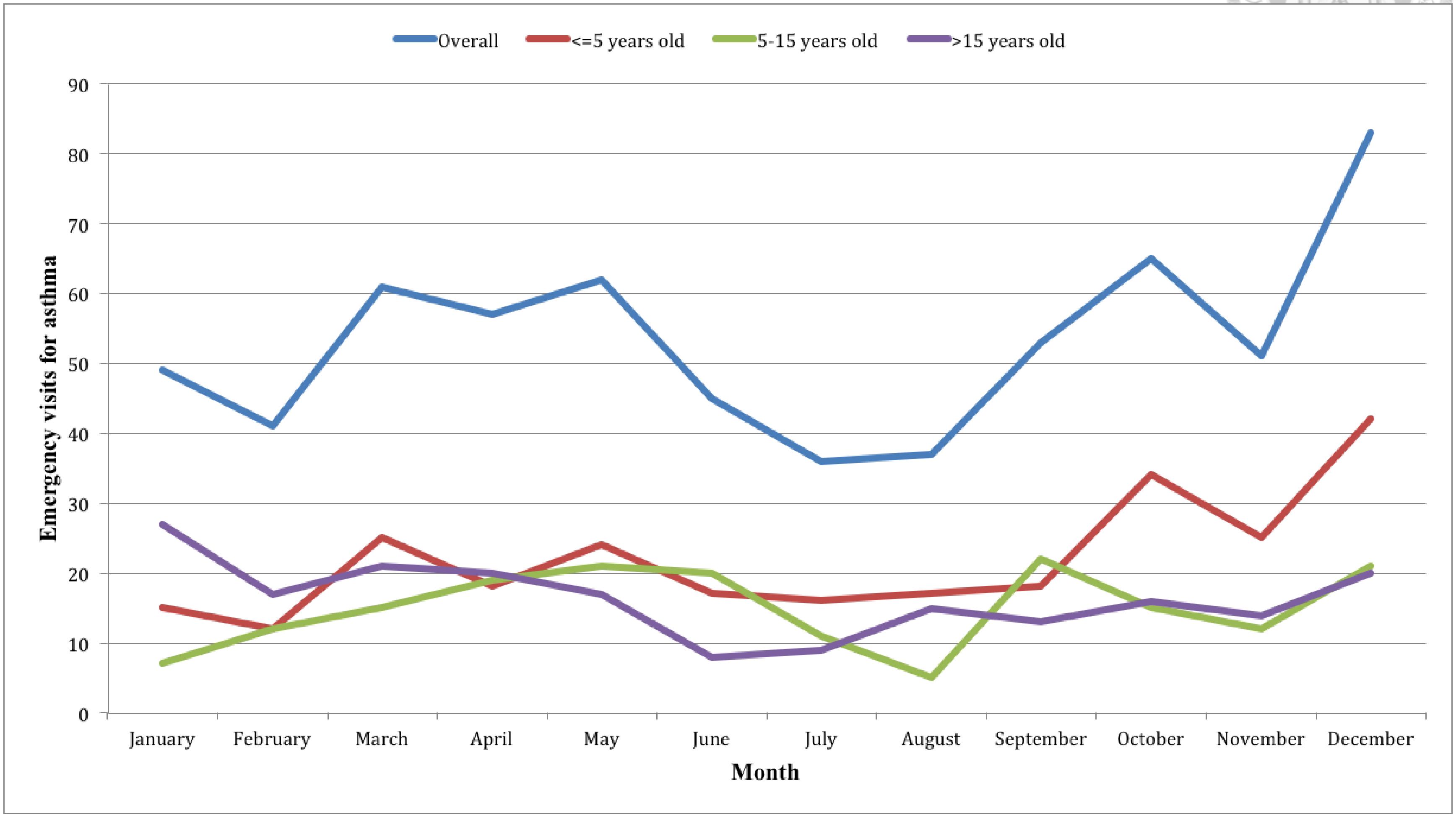
doi:10.6342/NTU201602867

Figure 2 Temporal trend of total fungal spore concentrations and monthly average of emergency asthma visits in NTUH in 2015



doi:10.6342/NTU201602867

Figure 3 Temporal variation of monthly average of emergency visits for asthma among different age groups in NTUH in 2015



doi:10.6342/NTU201602867