



Research article

Construction of polluted aerosol in accumulation that affects the incidence of lung cancer

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ABSTRACT

Background: This model demonstrated the correlation between lung cancer incidences and the parts of ambient air pollution according to the National Aeronautics and Space Administration (NASA)'s high resolution technology satellites.

Methods: Chemical type of aerosols was investigated by the Aerosol Diagnostics Model such as black carbon, mineral dust, organic carbon, sea-salt and SO₄. The model investigated associations between the six year accumulation of each aerosol and lung cancer incidence by Bayesian hierarchical spatio-temporal model. Which also represented integrated geophysical parameters.

Results: In analyses of accumulated chemical aerosol component from 2010 – 2016, the incidence rate ratio (IRR) of patients in 2017 were estimated. We observed a significant increasing risk for organic carbon exposure (IRR 1.021, 95%CI 1.020–1.022), SO₄, (IRR 1.026, 95% CI 1.025–1.028) and dust, (IRR 1.061, 95% CI 1.058–1.064). There was also suggestion of an increased risk with, every 1 ug/m³ increase in organic carbon compound is associated with 21% increased risk of lung cancer, whereas a 26% excess risk of cancer per 1 ug/m³ increase in mean SO₄ and 61% increased risk of lung cancer for dust levels. The other variables were the negative IRR which did not increase the risk of the exposed group.

Conclusion: With our results, this process can determine that organic carbon, SO₄ and dust was significantly associated with the elevated risk of lung cancer.

1. Introduction

Air pollution has a direct impact on our environment by disturbing its balance, causing greenhouse effects, global warming, and climate changes; changes that affect health. The characteristics of ambient air pollution contains several kinds of harmful contaminants that are breathable particles and cause particulate matter of various sizes. PM_{2.5} is a particle size not exceeding 2.5 microns (PM_{2.5}). PM₁₀ are larger particles. Both sizes are classified as one of the 5 main air pollution types besides sulfur dioxide (SO₂), nitrogen dioxide (NO₂), carbon monoxide (CO), ozone gas (O₃) [1]. More than 90% of the world population faced to the air quality levels exceed World Health Organization (WHO) standard [2]. Ambient air pollution exposure caused as many deaths as 4.2 million worldwide every year [3].

Air pollution problems can occur from many reasons. For example, the occurrence of acid rain with high levels of nitric and sulfuric acid.

These acids made up smog. In some instances, the dry precipitation characteristics may stem from gas and particulate. Ozone in the stratosphere layer protect the world from dangerous ultraviolet rays, which are different from the ozone at ground level. Ozone at ground level is another component of air pollution which is harmful to health and is the main ingredient of smog. The ozone is a chemical reaction between oxides of nitrogen and volatile organic compounds (VOC), with sunlight being a contributor to the reaction [4]. The pollution can affect our wellbeing, the diseases of respiratory tract such as asthma, or allergies [5, 6, 7, 8], chronic lung diseases [9], an important trigger of inflammation in autoimmune disease [10], cardiovascular diseases [11, 12], developmental defects of childhood such as autism and cognitive development [13, 14, 15], neurological disorders [16], mental health disorders [17, 18], and cancer [1, 19, 20].

Cancer is extremely widespread amongst many people. WHO reported the most common cancer for both sexes in 2018 was lung cancer

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with a 11% new cases, and still the leading cause of death with 18.4% mortality rate [21]. The lifestyle risk factors play a major role in this rise. In 2013, outdoor air pollution was recognized as a cause for lung cancer by the International Agency for Research on Cancer (IARC) [22].

With the information on air quality regulations in Thailand [23], it is found that ambient air pollution has become a major problem and has a health impact on the population. There several causes of this, such as emissions from traffic, industrial plants, and biomass [24, 25, 26]. Efforts to control the amount of toxic substances require an air quality monitoring stations, which is still not enough [1]. But in reality, pollution can occur anywhere in the country, including different urban and rural areas. With the time trend related increased the incidence of lung cancer in Thailand. It may be correlated with the air pollution [27]. For this reason, there should be a tool that can monitor all areas simultaneously. An approach for structural formation of fine particulate matter risk was developed. This model demonstrated the correlation between lung cancer incidences and the components of ambient air pollution by high resolution technology of National Aeronautics and Space Administration (NASA)'s satellites [28]. Satellite-derived annual means for aerosol grids in order to track aerial pollution trends was collected by the Modern-Era Retrospective Analysis for Research and Applications, Version 2 (MERRA-2) [29].

2. Method

The objective of this research was to investigate the influence of ambient aerosol components in lung cancer incidences which was demonstrated by spatio-temporal variations. With two main data-banks from Thai population cancer data and NASA Earth Observatory information were integrated for establishing the valuable outcome.

The spatial variation was the method by examining the differences in the populations across space-time by using a Bayesian modeling methodology. This model may be used not only for cluster disease specific detection but also for searching the confounding or etiological risk factors [30, 31, 32].

2.1. Ethical considerations

Data were obtained from two public domains which were opened for the public to use under noncommercial purposes. None of the variables or data used in this study allowed the identification of individuals. Confidentiality in this study was considered together with the privacy consideration, where relevant. The obligation to protect and promote the non-disclosure of information imparted in a relationship of trust lies at the core of the concept of confidentiality. The study was reviewed and approved by the Khon Kaen University Ethics Committee for Human Research (HE 631103).

2.2. Data records

2.2.1. Geographic locations

The Geographical Information System (GIS) of Thailand's database was demonstrated by latitudes of 5.77434–20.43353 and longitudes of 97.96852–105.22908 [33]. Currently an average of 68 million people who lived within the 77 provinces compounded with a total of 513,120 km² (198,120 sq mi). Located in Southeast Asia, the country was divided into six regions with Bangkok as the capital in the central region. Apart from its tropical rainforest like climate. It is humid all year round all tear round as well [34]. This computerized dataset contains names of provinces based on latitude and longitude on the Geographic Coordinate System: GCS_WGS_1984.38 was able to link the accurate geographical locations which could flourish and use land data in a separate layers [35].

2.2.2. Cancer data

The cancer data is the national reference amongst the Thai population contains data regarding incidence of the lung cancer from the database of

the Strategy and Planning Division, Ministry of Public Health between January 1, 2017 to December 31, 2017. 273,816 lung cancer patients from a total of 4,301,953 cancer patients were included [26].

2.2.3. Satellite representative air quality data

The requisites for obtaining ambient air pollution data was a set of satellite-based gridded, ambient air database. That is Aerosol Diagnostics Model (tavg1_2d_aer_Nx), MERRA-2, NASA's satellite bases report. The MERRA-2 process was computed on a cubed-sphere grid and analysis algorithm model was characterized by controlling the variable for moisture used in recent versions of Grid-point Statistic Interpolation analysis system (GSI) [36]. Highlights of the MERRA-2 system performed detailed data analysis every 3 h and were able to identify parameters monitored. This data was utilized as the mean value for each substance monthly and controlled aerosol/climate and aerosol-weather interactions [36]. Chemical type of aerosols was investigated by the Aerosol Diagnostics Model such as black carbon, mineral dust, organic carbon, sea-salt and SO₄. With this satellite observations, it could estimate of the past state of aerosol evidence throughout Thailand at the same time as cancer incidences recorded. Which also represented an integrated geophysical parameters in the mean level of individual grid cells for every month from the year 2011–2017. The MERRA-2 data used in this study/project have been provided by the Global Modeling and Assimilation Office (GMAO) at NASA Goddard Space Flight Center.

2.3. Data and spatial analysis

In the primary phase, the process was investigated by individual datasets. Spatial epidemiology analyzed geographical data and lung cancer incidence rates, that explain variations each year. Cancer mapping has been constructed to clarify the provincial distribution of disease rates and identify areas with low or high rates of incidences. With the same amount of time, a spatially correlated temporal effects with polluted aerosol components throughout Thailand was defined.

The secondary approach developed a statistical models with a Bayesian hierarchical for assessing health risks. With class of models; Integrated Nested Laplace Approximations (INLA) could be utilized to estimate the random variables. With a highly flexible model, the INLA provided solutions for adjustable control factors to develop a model that fits well. The influence of chemical species such as black carbon, mineral dust, organic carbon, sea-salt, and SO₄ was modelled by yearly random intercepts. Potential ambient air risk factors implicated in the increase of lung cancer incidence were assessed through a linear relationship analysis between the number of lung cancer cases and the presence of the ambient air substance using a multiple regression and a Pearson correlation. The effects of different control parameters were conducted by a statistical test of posterior marginal distributions for parameters. We adjusted effects of potential confounding factors which might be influence to a model. These five chemical types were controlled with a subset of variables such as mean relative humidity (%), maximum temperature (°C), minimum temperature (°C), wind speed (m/s), and precipitation. The other confounding factor for health effect was mean household income [37]. The best-performing parameter combinations were reported with 95% confidence intervals for the incidence rate ratio (IRR). This approach developed by time ambient related aerosol exposure. The model was investigated associations between the six year accumulation of each aerosol and lung cancer incidence. The correlation between spatial designs of the individual risk and the incidence rate ratio of lung cancer were estimated using a Spatial-Bayesian inference with the following Poisson log-linear model.

$$\log(\mu) = \alpha + \beta x \text{ or equivalently, } \mu = \exp(\alpha + \beta x) = \exp(\alpha)\exp(\beta x)$$

Which can easily show that:

$\exp(\alpha)$ = effect on the mean of Y , when $X = 0$, which is μ .

$\exp(\beta)$ = The corresponding predictor variable has multiplicative effect of $\exp(\beta)$ on the mean of Y per unit increase in X , which is μ .

A consequence of the above is that:

- i. In case $\beta = 0$, then $\exp(\beta) = 1$, and the expected value, $\mu = E(y) = \exp(\alpha)$, and Y and X are clearly not correlated.
- ii. In case $\beta > 0$, then $\exp(\beta) > 1$, and the expected value $\mu = E(y)$ is $\exp(\beta)$ times larger than when $X = 0$
- iii. In case $\beta < 0$, then $\exp(\beta) < 1$, and the expected value $\mu = E(y)$ is $\exp(\beta)$ times smaller than when $X = 0$

Integrated nested Laplace approximation (INLA) was used to fit models to spatial data in a Bayesian context [38].

$$\eta = \alpha + \sum n_{fj} = 1f(j) + \sum n_{\beta k} = 1\beta k z_{ki} + \epsilon_i \eta = \alpha + \sum j = 1n_{ff(j)} + \sum k = 1n_{\beta\beta k z_{ki}} + \epsilon_i$$

- η : the linear predictor for a generalized linear model formula.
- u : a linear function of some variables.
- β : the effects of covariates.
- z and ϵ : an unstructured residual.

3. Results

The actual incidence rate of lung cancer at the county level during 2017 displayed incidence rate of 273,816 (per 100,000 population) from a total 4,301,953 cancer patients. Whereas in Table 1 demonstrated the baseline of accumulated chemical component from 2010 – 2016 which effected the cancer incidence on 2017.

With the Bayesian spatio-temporal model, the posterior distributions for the parameters were simulated using R-INLA software. The spatial distribution of the fit model is shown in Table 2. It represents the posterior means and posterior standard deviations of parameters with 95% Bayesian credible intervals (CI). These display the estimated marginals of the precisions of the prior variances for the random effects in the best-selected model of each components. The exposure of each substance was able to be controlled by spatio-temporal distribution and income effect could be demonstrated, every 1 $\mu\text{g}/\text{m}^3$ increase in organic carbon compound is associated with 21% increased risk of lung cancer, whereas a 26% excess risk of cancer per 1 $\mu\text{g}/\text{m}^3$ increase in mean SO_4 and 61% increased risk of lung cancer for dust level.

For Table 3, the significant risk probabilities associated with 77 provinces of Incidence Rate Ratio (IRR) on organic carbon component 1.021, 95%CI 1.020–1.022 with P value <0.001, whereas SO_4 , IRR 1.026, 95% CI 1.025–1.028 with P value <0.001 and dust, IRR 1.061, 95% CI 1.058–1.064 with P value <0.001. The other variables were the negative IRR which did not increased risk in the exposed group.

Figure 1 illustrates the distribution of diseases by spatiotemporal distribution in a grid consisting of 40767 cells ($3 \times 3 \text{ km}^2$ resolution) as a province scale. The spatial distribution of the aerosol remarkable sign manifests in different signs. In Northern parts showed a dense organic carbon, dust and SO_4 level, whereas a Southern parts demonstrated mild degree of aerosol concentration. These substances concentration was consistent with incidence of lung cancer. On geographic province scales, the pattern of incidence rate on mapping indicated that the northern areas were more dens with cancer.

4. Discussion

Airborne particulate matter (PM) is a common indicator for air pollution. There are several sizes of particulate matter such as, UFPs, PM_{10} , $\text{PM}_{2.5}$, PM_{10} . The major PM components are ammonium sulfate, ammonium nitrate, organic carbonaceous mass, elemental carbon and crustal material/dust [39, 40] and also is usually a complex mixture of particles constituted by insoluble metals, organic compounds including PAHs and polychlorinated biphenyls, biological components (allergens), microbial agents, and water [41]. Seasonal variations and sources of pollutants displayed that the concentrations variable of PM-bound PAHs [42, 43]. From 2016 the International Agency for Research on Cancer (IARC), which is a specialized cancer agency of WHO, classified particulate matter (PM), as carcinogen type 1 that is harmful to human beings [1]. These molecular compositions of organic aerosols can enter the human body via by skin, digestive tract or by breathing. Airborne pollutants are released into a continuously moving surface film and pass through pulmonary epithelial cells at terminal bronchioles [44].

Several studies worldwide have demonstrated that $\text{PM}_{2.5}$ is directly associated with lung cancer incidence and mortality. There was reported that the incidence rate of lung cancer increased by 36%, when the daily $\text{PM}_{2.5}$ increased by $10 \mu\text{g}/\text{m}^3$ [45]. PM represents a serious health threat by many avenues. It can initiate structural lung damage with thickened alveolar walls and decreased alveolar spaces [46]. PM is also to induce the exceeding of pro-inflammatory cytokines that provoke cell cytotoxicity which contributes to inflammatory cell infiltration, increased alveolar interval, and promoted capillary dilatation [47, 48]. Reactive oxygen species (ROS) production during inflammation occupies a role as a contributors in PM induced DNA hypermethylation [49, 50]. The other mechanisms involve cell cycle alterations by the deregulation of cell signaling pathways [51], cell autophagy [52], and apoptosis [53]. These all of actions promote mechanisms of carcinogenesis [54].

The studies have found that the involvement of PM and lung cancer in both PM_{10} [55, 56, 57], $\text{PM}_{2.5}$ [58, 59, 60, 61] mostly, but PM_1 or even UFPs are limited to very few studies. With an effective tool to monitoring PM or even species of PM will serve the purpose of this research, but there are no efficient ambient air quality monitoring ground stations in Thailand. Global Modelling and Assimilation Office (GMAO), NASA demonstrated the pattern to make real-time estimates and forecasts of aerosols in subcategories of sea-salt, dust, organic and black carbon and sulfate [62]. This research obtained more information from the data bank of NASA's technology and Thai 's health system based to classify the chemical profiles of PM in carcinogenicity. Due to their great benefits of the satellites giving complete and synoptic views of large areas in one image on a systematic basis because of their global monitoring with high resolution, is an important tool for estimating and mapping air pollution for long periods.

There were several studies that presented the long-term exposure to ambient air pollution increased significantly with lung cancer, but nobody knew the exact time-risk involved [58, 63, 64]. However, there were evidences that showed more than five year of exposure effected lung function impairment [65, 66]. This was why we tried to investigate more than 5 years for risk related lung cancer. The more important question is which component of PM strongly effected lung cancer? The knowledge that can demonstrate the real cause for development of the disease.

Table 1. Baseline accumulated chemical component from 2010 - 2016.

chemical component	Mean ($\mu\text{g}/\text{m}^3$) ³	sd ($\mu\text{g}/\text{m}^3$) ³	Median ($\mu\text{g}/\text{m}^3$) ³	Min ($\mu\text{g}/\text{m}^3$) ³	Max ($\mu\text{g}/\text{m}^3$) ³
black carbon	8.21	3.08	8.14	2.80	16.47
organic carbon	49.56	14.77	54.03	18.50	76.35
sea salt	119.37	93.92	73.24	26.93	402.88
dust	14.36	2.91	14.21	8.85	20.70
sulfate	26.11	8.38	28.53	9.40	39.28

Table 2. Posterior marginals for linear predictor and fitted values computed of lung cancer in Thailand by the aerosol components.

Fixed effects	Mean	SD	2.50%	50%	97.50%
Black carbon					
Intercept	9.441	0.002	9.436	0.243	0.245
Precision for Black carbon	0.243	0.001	0.241	0.189	0.191
Precision for income	-0.034	0.000	-0.034	-0.034	-0.033
Precision for spatial	-0.015	0.000	-0.015	-0.015	-0.015
Precision for temporal	0.036	0.000	0.035	0.036	0.036
Organic carbon					
Intercept	9.320	0.003	9.316	9.320	9.325
Precision for Organic carbon	0.060	0.000	0.059	0.060	0.060
Precision for income	-0.037	0.000	-0.037	-0.037	-0.036
Precision for spatial	-0.015	0.000	-0.015	-0.015	-0.015
Precision for temporal	0.039	0.000	0.038	0.039	0.039
Sea salt					
Intercept	9.981	0.002	9.978	9.981	9.985
Precision for Sea salt	-0.010	0.000	-0.010	-0.010	-0.010
Precision for income	-0.040	0.000	-0.040	-0.040	-0.040
Precision for spatial	-0.015	0.000	-0.015	-0.015	-0.015
Precision for temporal	0.026	0.000	0.025	0.026	0.026
Dust					
Intercept	9.538	0.003	9.532	9.538	9.544
Precision for Dust	0.109	0.001	0.107	0.109	0.111
Precision for income	-0.037	0.000	-0.037	-0.037	-0.037
Precision for spatial	-0.015	0.000	-0.015	-0.015	-0.015
Precision for temporal	0.035	0.000	0.034	0.035	0.035
SO₄					
Intercept	9.133	0.003	9.128	9.133	9.139
Precision for SO ₄	0.144	0.000	0.143	0.144	0.145
Precision for income	-0.036	0.000	-0.036	-0.036	-0.036
Precision for spatial	-0.014	0.000	-0.014	-0.014	-0.014
Precision for temporal	0.046	0.000	0.046	0.046	0.047

Form our result, three components that effect the positive IRR and this supports the associations between components of aerosol and lung cancer. Though, organic carbon, dust and SO₄. also produced a great risk for lung cancer, but black carbon provided negative IRR risk which did not increased the risk in the exposed group. Sulfate or SO₄ represented like yellow smog that converted from SO₂ in high humidity and low temperatures situation [67]. Organic carbon (OC) and black carbon (BC) are the major components of PM_{2.5} and PM₁₀ [68]. The important chemical component in carbonaceous aerosols is polycyclic aromatic hydrocarbons which is the carcinogen [69] and exposures to polycyclic aromatic hydrocarbons found increased risks of lung and bladder cancers [70, 71]. From our investigation, black carbon was less effected like organic carbon. In the appropriate chemical combinations may achieve synergistic effects beyond an individual substance. The one found that at low concentrations of the accompanying treatment of inorganic and organic carbon in PM₁₀ and SO₂ led synergistic effect in the over-expression of decreased cell survival and apoptosis circumstance. While

alone, at the same concentrations PM₁₀ and SO₂, did not cause damage to the cells [72]. Some epidemiological studies have demonstrated a correlation between SO₂ inhalation and the occurrence of lung cancer in humans [73, 74]. SO₂ effected the airway epithelial cell function and caused airway dysfunction [75]. In addition to induce a cell apoptosis, SO₂ also enhanced an interactive feature on benzo(a)pyrene to cause apoptosis [76]. Furthermore, the basic and reliable polluted data collections are ground station monitoring but there must be enough stations in each country. This is the reason why we need to find other solutions such as satellite-based remote observations. With the several limitation of the inability to incorporate individual information made unadjusted effects for smoking prevalence, or even population dynamics of migration which might be interfered by the analysis result.

Thailand's air pollution policy, government official program established since 1997. With the strategies to reduce air pollution from many sources and also implement the regulations and law. The rationale for implementing the policy was a measurable to health and life benefits

Table 3. Comparison of accumulation levels in each aerosol component for geographic weighting regressions from 2011 to 2016 which demonstrated for lung cancer estimated incidence rate ratio in 2017.

	IRR	95% CI	p-value
Black carbon	0.926	0.924–0.928	<0.001
Dust	1.061	1.058–1.064	<0.001
Organic carbon	1.021	1.020–1.022	<0.001
Sea salt	0.999	0.999–0.999	<0.001
SO ₄	1.026	1.025–1.028	<0.001

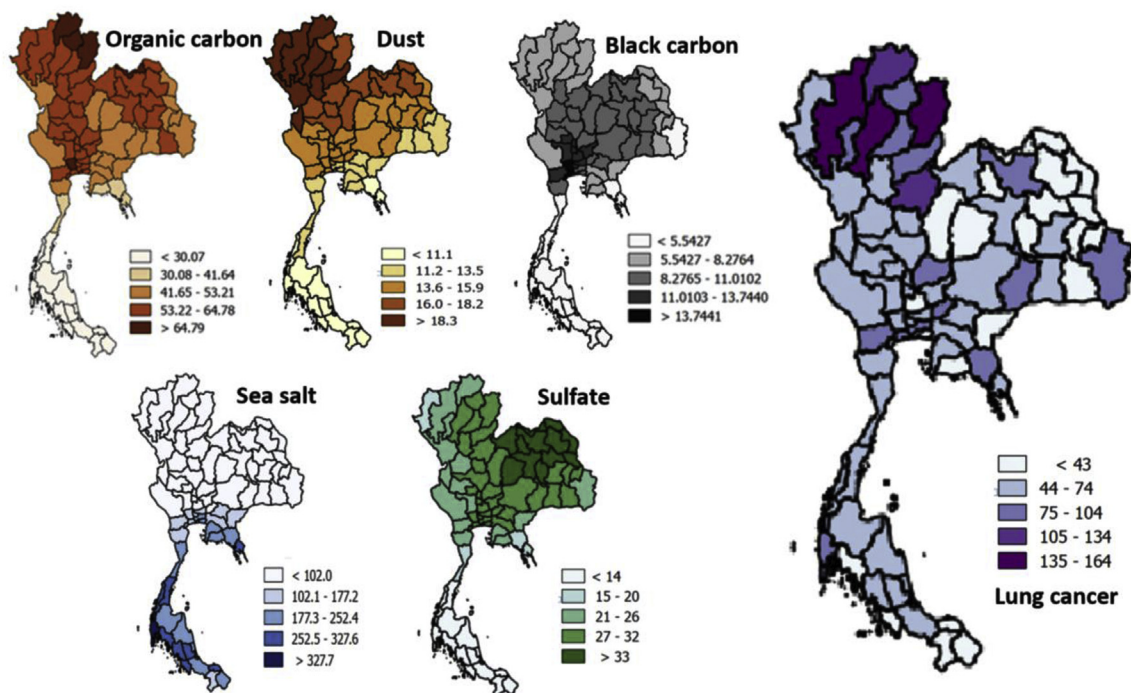


Figure 1. Spatial distribution of estimated comparison between lung cancer incidence and more than 5 years cumulative aerosol substances exposure.

[23]. However, estimating the effect of this policy on the healthcare system outcomes appear complicated. This project was the evidence support to push forward air quality improvement.

5. Conclusion

The intent of this research was to evaluate the influence of ambient aerosol components in lung cancer incidence with a long-term monitoring of species in aerosol component that covering data throughout Thailand. With our results, this process can determine that organic carbon, dust and SO_4 significantly correlated with the elevated risk of lung cancer. It also can represent visual perception with combination of Bayesian spatio-temporal models. This evidence provided an update data for the intervention policy to improve air quality. The limitations of the study are due to inaccessible of the individual information, such as social factors, co-morbidities, other risk factors or even population migration.

Declarations

Author contribution statement

Kriangsak Jenwitheesuk, Kamonwan Jenwitheesuk: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Udomlack Peansukwech: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

Additional data available on request please contact Kamonwan Jenwitheesuk; kamoje@kku.ac.th.

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