Title: The Impact of Long-term Air Pollution Exposure on COVID-19 Severity

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### Abstract

Since the emergence of the COVID-19 pandemic, long-term exposure to air pollution has emerged as a possible risk factor for increased COVID-19 disease risk, severity, and mortality. The objective of this study was to examine the association between COVID-19 and estimates of long-term exposure to air pollution at the census tract level.

This retrospective cohort study at an urban academic medical center included patients with air pollution exposure estimates testing outcomes for COVID-19 from March 18, 2020, to March 30, 2021. Air pollution exposure was assessed using models developed for Chicago by the MESA Air Study and data from the Environmental Protection Agency's EJSCREEN. Air pollution exposure estimates were linked to the University of Chicago Medicine patients using residential addresses. Air pollution measurements included PM2.5 (MESA Air and EPA), NO2, diesel PM, the respiratory hazard index, traffic proximity, and ozone. The outcome was COVID-19 risk, severity (ICU admission), and death. Mixed effect analyses were performed to test whether poor air quality status was associated with COVID-19 risk, severity, and mortality, controlling for demographic, smoking, and comorbidity indicators collected from the medical records.

A total of 74,004 patients (mean [SD] age 44.0 [22.51] years; 42,979 [58.09%] women; and 32,870 [49.09%] African Americans) were linked to air quality exposure based on residence and other covariates using electronic medical record data in addition to COVID-19 test results. Overall, 8,463 participants (11.4%) tested positive for COVID-19. In the mixed effect analysis, increasing PM2.5 exposure was associated with testing positive for COVID-19 (odds ratio [OR], 1.30; 95% CI, 1.23-1.38; P <0.01) and severity (OR= 2.28; 95% CI, 2.00-2.60; P = <0.01). The environmental risks differed between African Americans and the rest of the study population.

In this single-center, retrospective cohort study, poor air quality was associated with increased COVID-19 risk and severity. Combining individual-level data on COVID-19 with high-resolution air pollution data, we show a clear link between long-term exposure to air pollution and COVID-19 in Chicago with differences by race.

# Effect of Cord Blood Levels of Lead, Arsenic, and Zinc and Home Environment on Neurodevelopment in Children Aged 0 to 36 Months: A birth cohort study in Chitwan Valley, Nepal

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**Background:** Inconsistent results are continuously reported in studies linking low-level prenatal lead exposure and child development. Because of limited earlier epidemiological studies with birth cohort follow-up design, it remains inconclusive whether the associations of cord blood levels of toxic and essential elements, and postnatal raising environment on neurodevelopment of children remains constant throughout childhood or change over time.

**Aims:** This study aimed to investigate the influence of *in utero* toxic [lead (Pb) and arsenic (As)] and essential elements (zinc [Zn]) on the neurodevelopment of young children in Chitwan Valley, Nepal, considering the postnatal environment.

**Study Design and Subjects:** In this birth cohort study, participants (N=100 mother-infant pairs) were recruited in the Chitwan district, Nepal. We measured Pb, As, and Zn concentrations in the cord blood. The postnatal environment (i.e., home score or home environment) was evaluated using the Home Observation for Measurement of Environment (HOME) scale. The neurodevelopment of infants was assessed using the Brazelton Neonatal Behavioral Assessment Scale, third edition (NBAS III) at birth, and the Bayley Scale of Infant Development, Second Edition (BSID II) at ages 6, 24, and 36 months. Multivariate regression was performed to determine the association between *in utero* toxic and essential element levels and home environment with neurodevelopment scores adjusted for covariates. **Results:** Among the seven clusters of NBAS III, the motor cluster score was inversely associated with the state regulation cluster score. Cord blood levels of Pb, As, and Zn were not associated with any BSID II cluster scores in 6-, 24- and 36-month-old children. The total HOME score was positively associated with the psychomotor development index (PDI) score at 6 months and with the mental development scale (MDI) score at 24 and 36 months.

**Conclusion:** Low Pb and As exposure during the prenatal period may induce retardation of *in utero* neurodevelopment, but this effect disappeared when the child grew (i.e., 6, 24, and 36 months). The consistent beneficial effect of a stimulating home environment on neurodevelopmental indicators continues throughout early childhood.

These cohort babies are being followed after 14 years to see the effect of "peri-natal" (*in utero* and postnatal) exposure of Pb and As, together with other developmental adversities on overall intelligence quotient (IQ).

### Title: Diet Manipulation of Gut Microbiota Influences Food Behavior

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### Introduction:

Eating is one of the most fundamental and iconic human behaviors. Human food selection behavior is governed by a multitude of factors, including metabolic, psychological, and cultural factors. The nutritional transition from eating a paleolithic diet rich in lean protein with a wide variety of fruits and vegetables to eating a contemporary diet high in sugar, fat, salt, and processed foods has negative implications on human health. The chronic consumption of palatable foods has shifted our system from homeostatic (energy homeostasis) to hedonic (reward-related) eating. This shift is manifested by an increase in the obesity rate and a range of dysfunctional eating behaviors. The present interventional study aimed to explore the causal relationship between current food choices and future food preferences through the modulation of gut microbiota.

### Materials and methods:

Twelve specific pathogen-free (SPF) mice were subjected to a two-week dietary intervention to produce two distinct gut microbiota profiles. The control group (CONT) mice received standard AIN93M chow, and the treatment group (INU) mice received a high fiber inulin diet. All mice were placed individually in a customized cage for a food preference test for three days where mice could choose freely between a highfat (HF) diet or a high-sugar (HS) diet. Feed intake for both test diets was recorded at the start and end of the food preference test. Fecal samples were collected before and after dietary intervention to investigate the impact of inulin on gut microbiota composition; intermediate fecal sampling was also conducted to track the temporal changes in microbial composition. Welch's t-test was conducted on feed intake to determine the presence of food preference in CONT and INU group mice. 16S rRNA high-throughput gene amplicon sequencing was performed on the extracted bacterial DNA from the fecal samples. Food preference test results and 16S rRNA results were checked for statistically significant correlations using the Spearman correlation test.

### Results:

INU group mice exhibited a clear preference for fat and suppressed appetite for sugar (p<0.01) in the 3-day food preference test. In comparison, the CONT group did not exhibit any food preference. The CONT and INU groups had a similar total energy intake (INU consumed 4% less than CONT). The16S rRNA data showed distinct microbial compositions in the CONT and INU groups. The INU group exhibited less bacterial diversity than the CONT group (p<0.05). The Wilcoxon rank-sum test showed that *Bacteroides acidifaciens* and *Lactobacillus taiwanesis* were enriched in the INU group. The Spearman correlation test showed that *Bifidobacterium pseudolongum* was positively correlated with fat preference. These OTUs are key bacterial candidates that could potentially influence food preference through gut-brain axis communication.

### Conclusion:

The present study indicated that dietary composition has a causal effect on future food preferences. This causal relationship could be potentially modulated by gut microbiota. Further investigation is needed to confirm the role of gut microbiota in food preference.

# Changes in Spatial Patterns of Population Aging: A comparison between Japan and the Philippines

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The older population, as well as the impact of population aging, is not evenly distributed across and within countries. Understanding the geographic distribution of older people and their longitudinal changes will be important in meeting their changing needs in terms of health and social services, transportation, and housing, among others. We constructed a four-period panel dataset at municipal level using the population census in Japan and the Philippines from 2000 to 2015. We used the method proposed by Shiode et al. (2014), which aims to identify the types of aging communities in relation to the association between the proportion of older people and the number of older people in neighboring areas. We employed Bivariate Local Moran's I and examined the changes in spatial patterns of four types of aging communities: concentrated aged, non-aged, semi-aged, and depopulated aged. Concentrated aged municipalities have a high proportion of older people and have neighboring municipalities with a high number of older people, while non-aged municipalities have a low proportion of older people and have neighbors with a low number of older people. Semi-aged municipalities have a low proportion of older people and neighboring municipalities with a high number of older people. Depopulated aged municipalities have a high proportion of older people but have neighbors with a low number of older people. We also investigated the spatial association between the change in number and in the proportion of the older population in 2000--2015 using Bivariate Local Moran's I. The results show that depopulated aged municipalities are widespread in Japan, but mostly in Hokkaido. The depopulated municipalities in Aomori, Miyazaki, and Kumamoto are expanding. Pockets of nonaged municipalities were found in Hokkaido, Fukushima, and Nagano. Semi-aged municipalities are located in metropolitan areas in the Kanto and Kansai regions, with pockets of concentrated aged municipalities around it. These communities are rapidly increasing in number and proportion. In the Philippines, non-aged municipalities are in the north- and southwestern regions of the country. Depopulated aged municipalities are found in the north-west and east central regions of the Philippines; some are diminishing and expanding over time. Similar to Japan, most semi-aged municipalities are found in the Greater Manila Area with surrounding pockets of concentrated aged municipalities that are expanding over time. These non-aged and semi-aged municipalities have the fastest growth in both numbers and proportions. The findings highlighted that although highly urbanized areas are semi-aged, the suburbs around it are where aging is becoming concentrated, both in proportion and in numbers. If the above trend continues, the delivery of services might be affected.

The secret of the deliciousness of miso nikomi udon:From the effect of multiple umami

### intertwining

味噌煮込みうどんの美味しさの秘密;複数の旨みが絡み合う効果から

# Nozomu Okada (Misonikomin) 岡田 望(味噌煮込罠)

味噌煮込みうどんは愛知県を中心に中京地方で親しまれている郷土料理である。起源は諸 説あるが、山梨県のほうとうが伝わったとされる説が有力である。 味噌煮込みうどんが他の うどんと異なる点は『うどんを味噌で溶いただしの中で煮込む』というものである。塩を使 わずに打ったうどんを生に近い状態から味噌だし中で煮込み、独特のゴワッとした食感と 濃厚な味が特徴である。 ベースの味はこの地方で多く作られる豆味噌で、 原料のうち大豆の 割合が多いこと、熟成期間が長いことによりアミノ酸生成量が米味噌・麦味噌に比べ非常に 多く、強い旨味、酸味や香気成分を有する。そして、旨味を強く感じる最も大きな理由は味 噌とだし、具材を一緒に煮込むことにより旨味の相乗効果を引き出している点にある。旨味 物質にはグルタミン酸ナトリウム、イノシン酸、グアニル酸の3つがあり、それぞれ昆布だ し、カツオだし、干し椎茸のだしの主成分である。このうちグルタミン酸とイノシン酸を1: 1の割合で共存させると旨味が7~8倍になるというデータがある。グルタミン酸を認識し た旨味受容体がイノシン酸と接触することでグルタミン酸が遊離しにくくなり、旨味を強 く感じさせることが分かっている。 またグアニル酸は旨味受容体を変形させ、 グルタミン酸 をより長時間保持させる作用がある。これらを踏まえると味噌煮込みうどんは昆布と干し 椎茸、カツオ等の魚介系だしから3つの旨味成分を抽出し、そこへグルタミン酸が豊富な味 噌や鶏肉などの具材を加え煮込むことで最終的に非常に強い旨みを呈することが分かる。

### Title:

Food store accessibility affects nutritional intake through shopping frequency and food intake in middle-aged to older adults in rural Nagasaki, Japan

### Abstract:

### Objectives

The food environment is an important determinant of dietary and nutritional intake, but studies have reported mixed results. We examined the associations between food store accessibility and nutritional intake among middle-aged to older adults in rural areas in Japan.

## Methods

We conducted a questionnaire survey in three municipalities in Nagasaki, Japan, for those aged 40– 74 years. By using location data and a telephone directory database, direct distances from home and food store density were estimated using a geographic information system (GIS). We focused on protein, vitamin D, and calcium intake for their preventive effects on frailty and sarcopenia. To examine the effects of food store accessibility on nutritional intake, we hypothesized a model with a chain of associations between food store accessibility, shopping frequency, food intake frequency, and nutritional intake. We performed path analyses to explore the food items to be included in the models, associations between the variables, and fitness of the models.

### Results

We obtained final models with satisfactory fit indices. The resultant models included significant associations between accessibility indicators and shopping frequency, shopping frequency and intake frequency for two or four categories of food, and intake frequency and nutritional intake. Conclusions

The results demonstrated that accessibility to food stores, assessed in terms of direct distance from home and food store density, can affect the intake of protein, vitamin D, and calcium through the effect on shopping frequency and intake frequency of some categories of food items among middleaged to older adults in Nagasaki, Japan.

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