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Cover design

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Editorial office

Premier Publishing s.r.o. Praha 8
– Karlín, Lyčkovo nám. 508/7, PŠČ 18600

E-mail:

pub@ppublishing.org

Homepage:

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Section 1. Biology

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Yiran Deng,

Professional Children's School, Chinese
New York, NY, United States of America

E-mail: ydeng3373@gmail.com

Dr. Dun Yang,

Professor, J. Michael Bishop Institute
of Cancer Research, Chengdu, China

THE MBICR-20 COMPOUND INDUCE MINIMIZED NUCLEI DEATH

Abstract. Current cancer therapies mainly treat cancer by inducing cell apoptosis. However, tumor cells exhibit anti-apoptotic activity, so they develop drug resistance. We adopt a new approach to cancer therapy to overcome this, turning multi-layer cells and cells that do not have contact inhibition back to nearly normal.

Keywords: Autolysosome, chloroquine, hepatocarcinoma, immunofluorescent staining, MYC Nick HCC, PI staining, nuclei, vacuole.

Introduction

My experiments were conducted on the MYC Nick HCC cell line. The cell line is a hepatocarcinoma cell line derived from mice, which overexpress MYC oncogene and MYC Nick gene.

Among all drugs we tested brought from the market, to use the old medicines for a new use or through the later organic transformation and modification, drug MBICR-20 was found to form vacuoles and ultimately induce minimized cell nuclei.

Furthermore, we tested the relation between the formation of vacuoles to autolysosomes after we detected acidic vehicles accumulating in the vacuole's membrane and around the vacuoles.

Methods

Cell lines and cell culture

The experiments were conducted on MYC Nick HCC. The MYC Nick HCC is a Hepatocellular car-

cinoma model cell line added with over-expressed MYC Nick.

Cells were cultured at 37 °C and 5% of CO₂ in DMEM (Gibco, Cleveland, TN, USA) supplemented with 5% fetal bovine serum (Gibco), penicillin (100 U/mL)-streptomycin (100 µg/mL) (Gibco, 15140-122), 2 mM glutamine (Gibco, 200 mM solution, 25030081) and 1 mM sodium pyruvate (Gibco, 100 mM solution, 11360070).

PI Staining

Aspirate cell medium, wash with 1xPBS, fix in 4% paraformaldehyde (PFA) for 10 minutes, 0.5% Triton X-100 for 10 minutes, apply Proidium Iodide, and RNaseA (1:200) dilution, wash with 1X PBS, and add 250 ml PBS to each well. Then observe cell density under Evos FL Autofluorescence microscope.

Immunofluorescent staining

Immunofluorescent Staining MYC Nick HCC cells were cultured on coverslips coating with 0.1%

gelatin in a six-well plate and allowed to adhere overnight at 37 °C. After exposure to the chemicals described in the figure legends for the indicated times, the cells were washed with PBS once, fixed with 4% of paraformaldehyde (PFA) for 10 min in the presence of 0.5% of the detergent TritonX-100, and then were incubated with 5% BSA blocking buffer for 1h at room temperature. Immunofluorescent staining procedures were typically performed by incubation with a primary antibody for two hours at room temperature and then a FITC or Rhodamine-labelled secondary antibody for one hour at room temperature. Finally, cells were counterstained with

DAPI in the VECTOR or Yeasen mounting media and observed under the Evos FL Autofluorescence microscope (ThermoFisher).

First Antibody: LAMP1 (D2D11) XP® Rabbit mAb #9091 (CST)

Second Antibody: Rhodamine (TRITC) Affini-Pure Goat Anti-Rabbit IgG (H+L) Jackson

Results

Vacuole Formation, Reduced Cell Density, and Minimized Nuclei

After treatment of MBICR-20, vacuoles formed. The vacuole has the ability to reduce surrounding cell density (figure 1), and destroy cell nuclei (figure 2).

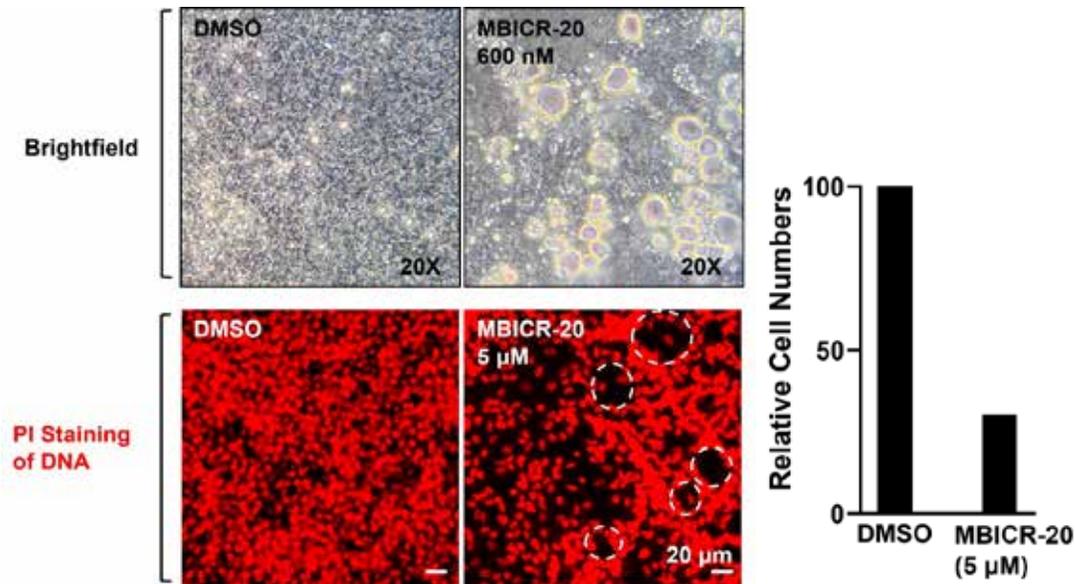


Figure 1. Result of MBICR-20 drug treatment presented by software ImageJ after PI staining. (Brightfield) Vacuole form in MYC Nick HCC cells. (PI Staining of DNA) Vacuole form and cell density reduced

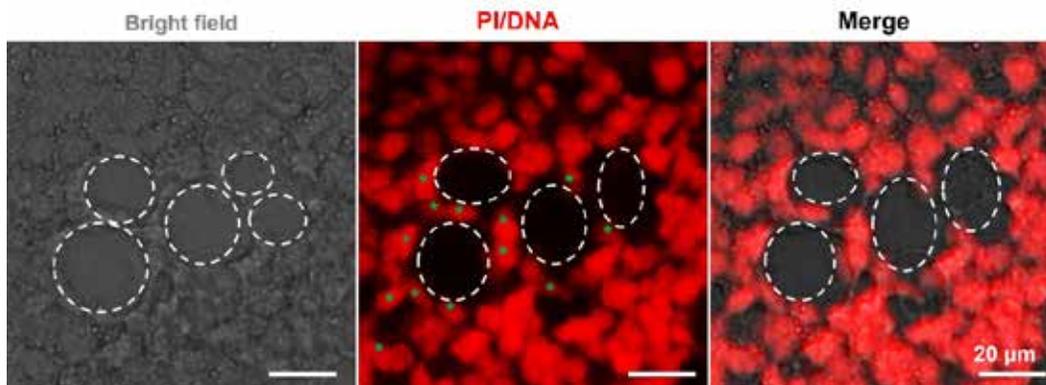


Figure 2. Vacuole degrades surrounding cells, eventually destroying nuclei in contact with the vacuole, killing the cells and reducing the number of cells.

Acidic vehicles are concentrated around the periphery of vacuoles and in the vacuole

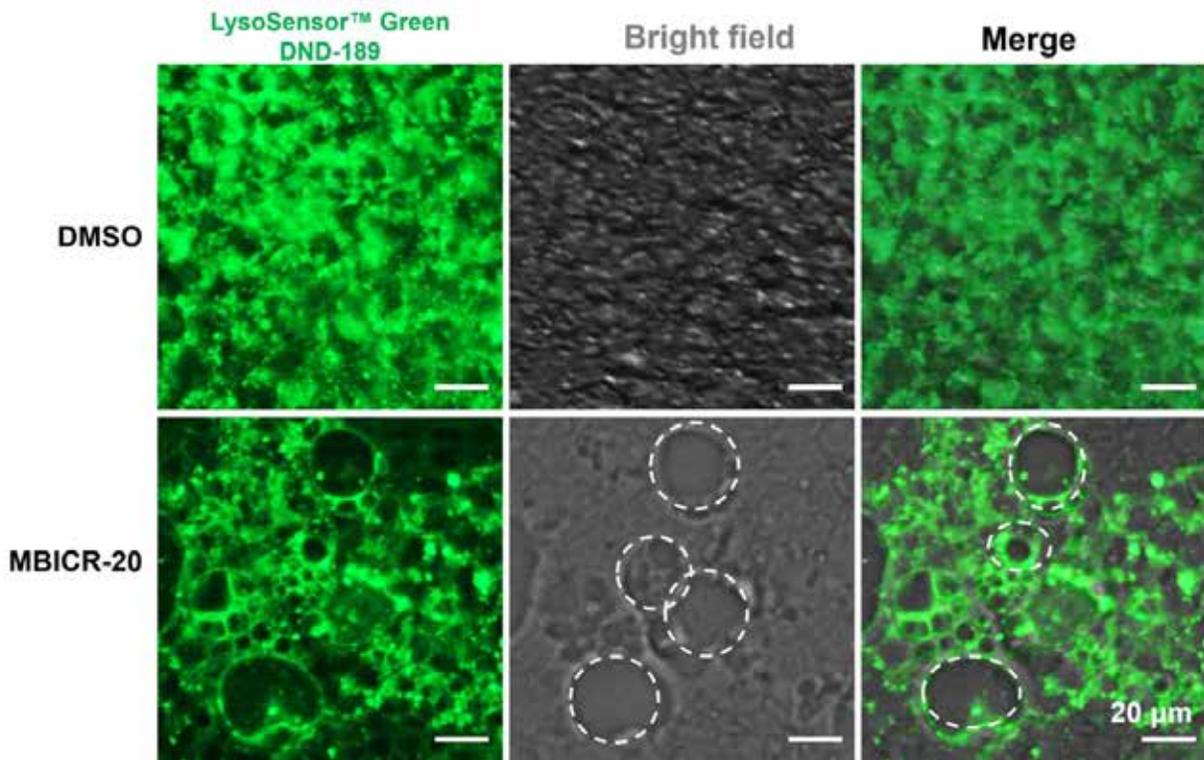


Figure 3. Result after applying LysoSensor Green DND-189

Many acidic substances were found gathered around the vacuole membrane and the vacuole itself, after applying LysoSensor Green DND-189, an acidic dye that could attach to the vacuole membrane.

Lamp 1 Accumulate in The Vacuole's Membrane and Around the Vacuoles

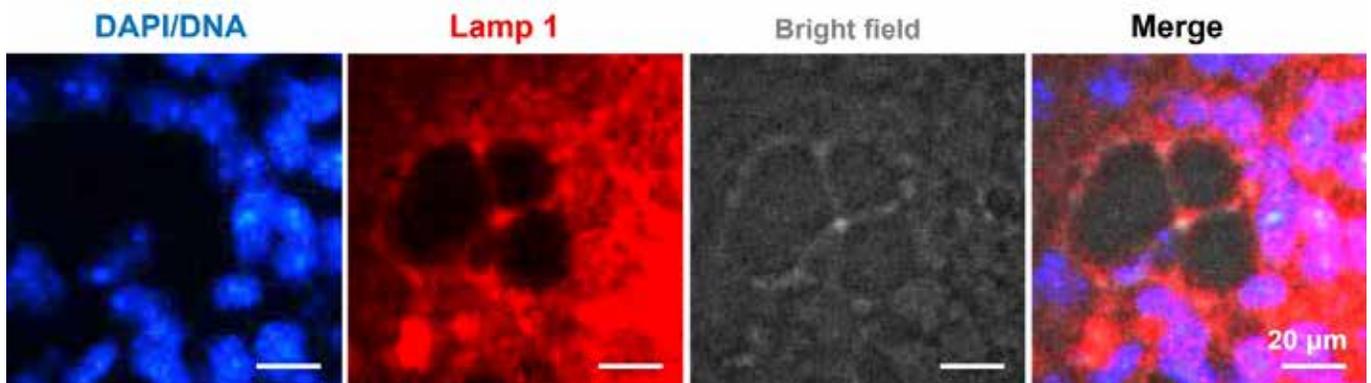


Figure 4. Results of Immunofluorescent staining of lysosome marked by protein Lamp 1

In this experiment, we can see that the number of proteins Lamp1 gathered around the vacuole. Therefore, the result of cell density reduction led by degradation of the nucleus associated with vacuole formation and minimized nuclei might be related to autophagosome.

m Torc 1 inhibits the ULK complex, which disables VPS34, forming a membrane of autophagosomes. Chloroquine inhibits the fusion of lysosomes and autophagosomes to form autolysosomes. Understanding the formation of vacuole is related to autophagosome, we used the inhibitor of

mTorc1 Rapamycin and Chloroquine to test if the drug needs active Chloroquine and m Torc 1.

m TORC 1 is Required for Vacuole Formation and Minimized Cell Nuclei

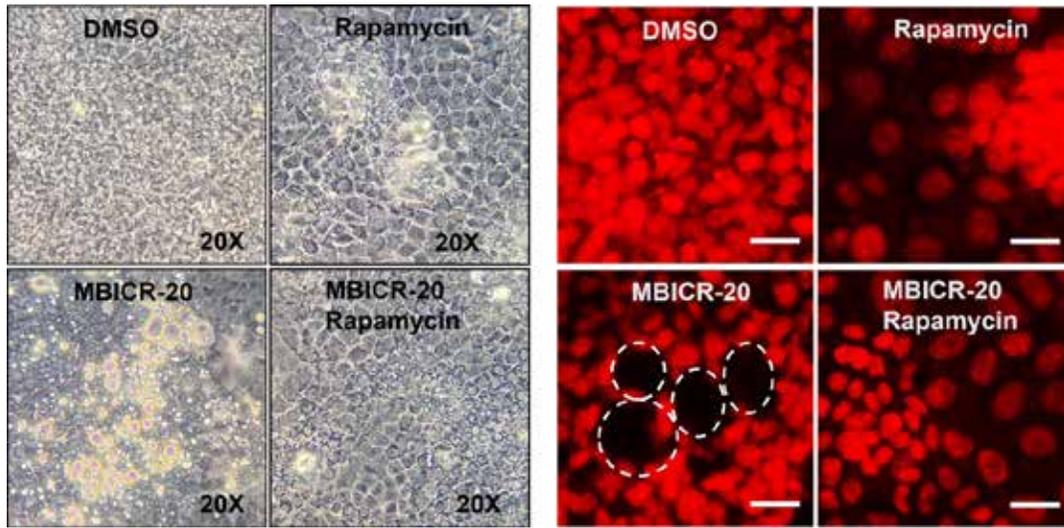


Figure 5. Result of treatment with Rapamycin and MBICR-20

m Torc 1 incepts autophagosomes and Rapamycin is the inhibitor of m Torc 1, so when Rapamycin was added, autophagosomes stopped. When Rapamycin was added with the MBICR-20, vacuole

did not form. This indicates that formation of the vacuole needs m Torc 1.

Autolysosome and Degradation Are Not Related to Vacuole Formation and Minimized Cell Nuclei

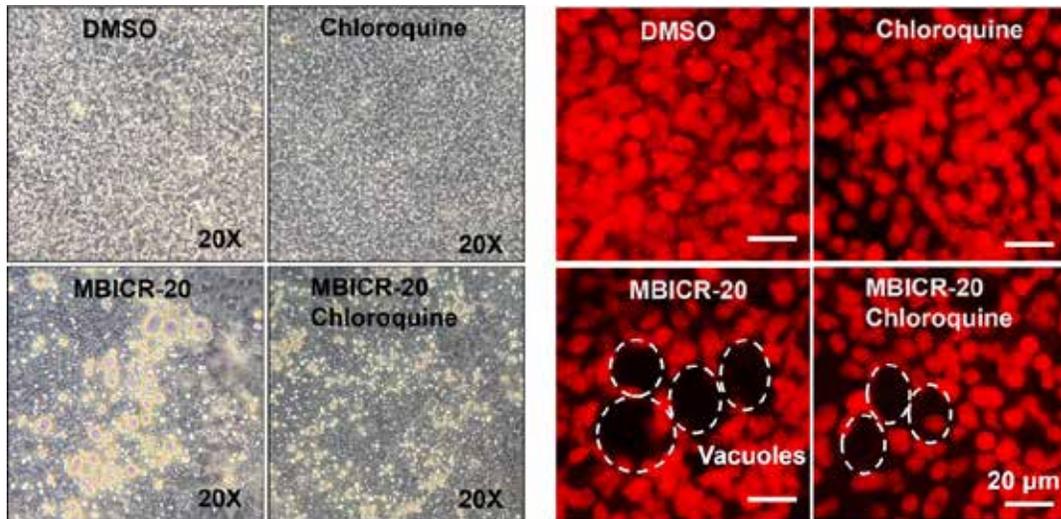


Figure 6. Results of treatment with Chloroquine and MBICR-20

Chloroquine inhibits the fusion of lysosomes and autophagosomes. In the process of autophagosomes formation, it combines with lysosomes and becomes autolysosomes. When cells were treated with Chloroquine and MBICR-20, vacuoles still existed. This finding shows that the formation of the vacuole is

not related to Chloroquine. Therefore, vacuole formation is not associated with autolysosome and its degradation.

Conclusions

Drug MBICR-20 achieved a new method for cancer therapy to transform cancer cells towards

normalization instead of inducing cell apoptosis. The formation and minimization of vacuoles require the regulation of mTOR protein. However, the process does not depend on mTOR-mediated autophagy. Meanwhile, vacuole and minimized nuclei do not depend on the formation of autophagy lysosomes. Beyond that, whether it is related to autophagy still needs further research.

Acknowledgement

With sincere appreciation, I would like to thank Dr. Dun Yang and Mrs. Betty Wang for giving me this opportunity to work at J. Michael Bishop Institute of Cancer Research. I would also like to thank Qiong Shi, Ziqi Yan, Zhengchi He, and especially my supervisor, Yan Long for their immense guidance and support that allowed me to design and analyze my experiments. This manuscript would not have been possible without their generous help.

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Yixuan Yun,
Forest Ridge of the Sacred Heart
Bellevue, Washington United States of America

Dun Yang,
Professor, J. Michael Bishop Institute
of Cancer Research, Chengdu, China
E-mail:

TARGETING OF AURKA, AURKB, AND MKLP2 BY GHG192 BLOCKS CYTOKINESIS

Abstract

Introduction. The MYC gene frequently exists in human cancer cells and plays an essential role in regular cell cycle progression, proliferation, differentiation, apoptosis, and cellular transformation. The MYC over-expression occurs and sometimes plays as a critical inducer in more than 50% of human malignancies. Thus, MYC represents a promising target for cancer treatments. It has been discovered that MYC is essential in normal cells and the therapeutic window of direct targeting is slim. Furthermore, directly targeting MYC oncoprotein has been proven to be inappropriate since it is difficult to be inhibited with pharmaceuticals due to its nuclear localization and lack of a classical active site. To exploit synthetic lethality for cancer over-expressing the MYC oncogene, a novel approach to cancer therapeutics called “the synthetic lethal therapy” is applied. The principle of MYC-synthetic lethality is that for low expression gene A with an inhibited gene B, the cell lives; whereas high expression gene A with inhibited gene B leads to cell death. In other words, when a protein is inhibited in the cell with low MYC expression, the cell lives. However, synthetic lethality is only achieved when the protein is inhibited with MYC overexpression.

Objective. Previous studies have discovered a synthetic lethal interaction between over-expression of MYC and AURKB; at the same time, AURKA plays an indispensable role in the regulation of cell division or chromosome segregation, and MKLP2 and AURKB have an ATP-binding pocket. Hence, we hypothesize that a compound that is either upstream or downstream of the AURKB might also kill the MYC expression. Based on this, we used AURKB, MKLP2, and AURKA to test the drug's efficacy, and further applied it in human cancer cell lines.

Methods. To screen for GHG192, a molecule library with 616 compounds was the first step for screening, using a high throughput screening with the RPE-MYC^{H2B-GFP} cells. By using an In-Cell analyzer 2000, we found the cells would eventually become polyploids after the inhibition. Then we applied the drug GHG192 into AURKA, AURKB, and MKLP2, to research for the reasons of cytokinetic failure.

Result. The Immunofluorescence staining revealed that GHG192 could elicit polyploidy and cytokinetic failure with the minimum concentration. By observing the model cells, AURKB, AURKA,

and MKLP2's activity could all be blocked with the minimum concentration of inhibition. This fact also proves GHG192 can inhibit their phosphorylation and cytokinesis. As the most crucial part, GHG192 can elicit cell death as associated with polyploidy formation in human cancer cell lines. Although it is unknown whether GHG192 has an effect either *in vitro*, that more human cancer cell lines or other mitotic regulators could elicit polyploidy in cells; or *in vivo*, there's efficacy and PK study in the mouse model and optimization in the structure to improve the potency of compounds.

Conclusion. While GHG192 highly shows effective elicitation of polyploidy and cytokinetic failure, it can also inhibit human cancer cell lines effectively, which can be concluded that GHG192 has the potential to serve cancer patients in future therapies.

Keywords: Synthetic Lethal Therapy, MYC-targeted Therapy, Immunofluorescence Staining, GHG192, MYC oncoprotein, Aurora A Kinase, Aurora B Kinase, MKLP2, Cancer line cell, Cytokinesis, polyploidy.

Introduction

Malignant tumors are great threats all over the world. The new cases of cancer incidence rate is about 442.4 per 100,00 for both men and women per year during 2013–2017; the cancer death rate is 158.3 per 100,000 for men and women per year during 2013–2017 (National Cancer Institute). Luckily, with the development of medical science, treatments for various malignant tumors have made relatively great progress. Some tumors even achieved high cure and survival rates, yet still have the possibility of high recurrence and metastasis rates. In order to eliminate the possibility, various type of therapies have been explored. It was found that in 50% of human cancers, MYC family oncogenes are out of control, and they are often related to poor prognosis and poor survival of patients. Traditional methods and modern therapeutics including surgical excision, radiotherapy, chemotherapy, oncoprotein targeted therapy, and immunotherapy have been proven unsuitable for cancer cells. MYC though plays an essential role in regular cell cycle progression, proliferation, differentiation, apoptosis, and cellular transformation, thus representing a promising target for treatments of cancer [1; 2].

In mammals, MYC gene family includes C-MYC, N-MYC, L-MYC, and S-MYC. Among them, C-MYC, L-MYC, and N-MYC are closely related to the occurrence and development of human tumors [3,4]. Studies have shown that the expression

of MYC gene in most tumors is significantly higher than in para-cancer tissues, which indicates that the high expression of MYC contributes to the development of tumors [5]. MYC Is a powerful proto-oncogene, originally found in the chromosome of Burkitt lymphoma. In normal cells, MYC proto-oncogene is strictly regulated by multiple regulatory mechanisms and signals transduction pathways at the transcription level, post-transcriptional level, cell cycle checkpoint and chromosome mitosis. These strict regulatory mechanisms prevent cells from becoming cancerous, and so far MYC is one of the most frequently unregulated oncogenes [2]. In mouse models, systemic knockout of MYC can significantly inhibit the occurrence and development of tumors, indicating that targeting MYC can be used as an option for tumor treatment [6]. Although the inhibition of MYC seems to be a particularly promising solution, because MYC is a transcription factor due to its special structures, it lacks the protein structure region that small molecule drugs bind to, and there are currently no small molecule drugs that could directly target MYC. Therefore, in order to achieve the ideal anti-tumor effect, people have widely explored alternatives to MYC blockade; and indirect targeting of MYC has become the most possible solution according to current research.

Aurora kinases are a class of serine/threonine kinases, composed of AURKA, AURKB, and AURKC

[7]. It comes to light that they play an indispensable role in the regulation of cell division and chromosome segregation. While AURKC is mainly expressed in meiotically active germ cells, AURKA and AURKB are ubiquitous and play an important role in mitosis. They are often found to be amplified or over-expressed in human cancers [8; 9]. AURKA encodes an evolutionarily conserved serine/threonine kinases, which is one of the Aurora kinases family members. In mitosis, AURKA participates in the separation and maturation of centrosomes and the establishment of spindle poles to ensure the correct separation of chromosomes and the smooth completion of cytokinesis during mitosis. It plays an important role in the cell cycle [10]. Abnormal amplification and /or high expression of AURKA are common in many human tumors. Recent studies have shown that AURKA can participate in a number of important cells signaling pathways, as a kinase, directly or indirectly activates a variety of oncoproteins, or inactivates a variety of tumor suppressor proteins, and thereby promotes the occurrence and development of tumors [10].

AURKB is a kind of protein that regulates chromosomal microtubule interaction, cohesion, spindle stability and cell division [11]. In addition to its role in the cell cycle, AURKB exerts its kinases activity to phosphorylate tumor suppressor and enhance its polyubiquitination and proteasome degradation [12], suggesting that AURKB has a non-mitotic tumor-promoting effect. It has been reported that AURKB is abnormally expressed in a variety of cancers and is positively correlated with poor prognosis [13]. MKLP2 is a significant protein that controls cytokinesis. Meanwhile the relocation of AURKB requires MKLP2 [14; 15]. Therefore, MKLP2 is also one of the essential links in the tumor genesis pathway.

Hence, we hypothesize that a compound that is either upstream or downstream of the AURKB might also kill the MYC expression. Based on this, we used AURKB, MKLP2, and AURKA to test the drug's efficacy, and further apply it in human cancer

cell line to observe the strength of the drug's effect. It is expected to be applied in the practice of animal carcinoma models and human cancer treatment in the future, hopefully playing a certain role in the overall treatment of cancers in various human organs.

Materials and Methods:

Chemicals

The molecule library is supported by J. Michael Bishop Institute of Cancer Research. It is composed of about 1000 chemicals, including drugs they bought from Selleck Chemicals, and drugs that are investigational. AURKB's specific inhibitor AZD1152 (Cat. No. S1147) and AURKA's specific inhibitor MLN8237 (Cat. No.1133) were all purchased from Selleck Chemicals, as many of their other drugs. All chemicals were dissolved in DMSO (CAS: 67-68-5, LOT: D103272) as a 1000x stock solution. The drug GHG192 was composed chemically.

Antibodies

Rabbit anti-Aurora A/AIK (phospho-Thr288) (Cat. No.3079) polyclonal antibody and rabbit anti-Histone H3 (phospho-Ser10) (Cat. No. 53348S) were obtained from Cell Signaling Technology, Inc. Rabbit Aurora B antibody (Cat. No. 131460) was obtained from Absin. Rhodamine (TRITC) AffiniPure Goat Anti-Rabbit IgG (H+L) (Cat. No. 111-025-003) was obtained from Jackson Laboratories. Mounting media containing 4',6-Diamidino-2-phenylindole dihydrochloride (DAPI) was obtained from Yeasen Institute of Biotechnology (Cat. No. 36308ES11) (Shanghai, China).

Cell Culture

The RPE series were derived from human retinal pigment epithelium and then stably transfected with an hTERT expression construct for immortalization. The resulting cell line was then transformed to the MYC overexpression and BCL₂ oncogene to emerge the RPE MBC cell line. Cells were cultured at 37 °C and 5% CO₂ in DMEM (Gibco, Cleveland, TN, USA) supplemented with 5% fetal bovine serum (Gibco, Cleveland, TN, USA), penicillin (100 U/mL)-streptomycin (100 µg/mL) (Gibco,15140-122), 2 mM

glutamine (Gibco, 200 mM solution, 25030081) and 1mM sodium pyruvate (Gibco, 100 mM solution, 11360070).

Immunofluorescent (IF) Staining

RPE MBC cells were cultured on a coverslip coating with 0.1% gelatin in a six-well plate, then adhered for a night at 37 °C. After exposure to RPE-MYC^{H2B-GFP} with 20 μM compound concentration, the cells were washed with PBS once, fixed with 4% of paraformaldehyde (PFA) for 10 min of 0.5% of the detergent TritonX-100, and then were incubated with 5% BSA blocking buffer for 1h at room temperature. IF staining procedures were typically performed by incubation with a primary antibody for 2h at room temperature and then a Fluorescein isothiocyanate (FITC) or Rhodamine-labelled secondary antibody for 1h at room temperature. Finally, cells were counterstained with DAPI in the VECTOR or Yeasen mounting media and checked under the Evos FL Auto fluorescence microscope (ThermoFisher).

MTT assay

For preparation, cell lines that we used were split when growing at the mid-Log phase. Cells in 100 μL of DMEM/1640 medium were seeded in one well in 96-well plates and cultivated for 15~24 hours to reach a confluence of 20~30% before the initiation of drug treatment.

For the drug treatment-series dilution, cells in 96-well plates were exposed to drugs at concentrations ranging from 1 nM to 1 μM. (compounds stock solution 200 μM in tube). 1 μL of the working solution was added to 200 μL of DMEM in a well in col-

umn 1 of a 96-well plate. Each well from column 2 to 12 contained 100 μL of DMEM. Series dilution from column 2 to column 12 was performed by transferring 100 μL of DMEM from column 1 to column 2 and the process was repeated for the remaining columns.

At the 3 days endpoint, we added 20 μL MTT (stock solution 5 mg/mL) to 100 μL DMEM, so the final concentration of MTT was 0.83 mg/mL. Then set at 37 °C with 5% CO₂ incubator for 3~4 h.

We then took the cell plate, aspirated the medium with a washer, added 50 μL DMSO to each well, and incubated with shaking for 10 min. we then placed the 96-well plate under the microplate reader and measured its OD value (A570) at a wavelength of 570 nm.

Results and Discussion

MYC-Synthetic lethality with disablement of AURKA, AURKB, MKLP2

Previous studies have discovered a synthetic lethal interaction between overexpression of MYC and AURKB (Yang et.al. [16]). The activity of MKLP 2, AURKA, and AURKB is essential for cytokinesis when all three mitotic regulators or either one is inhibited, leading to polyploid cells (Fig.1). To extend this study, we focused on the AURKB and MKLP2 signal pathway to screen and induced a synthetic lethal agent for MYC, so that this compound can prevent drug resistance that frequently exists in monotherapies. To achieve that, we reversed the strategy to find the phenotype of polyploid phenotype as the standard of screening.

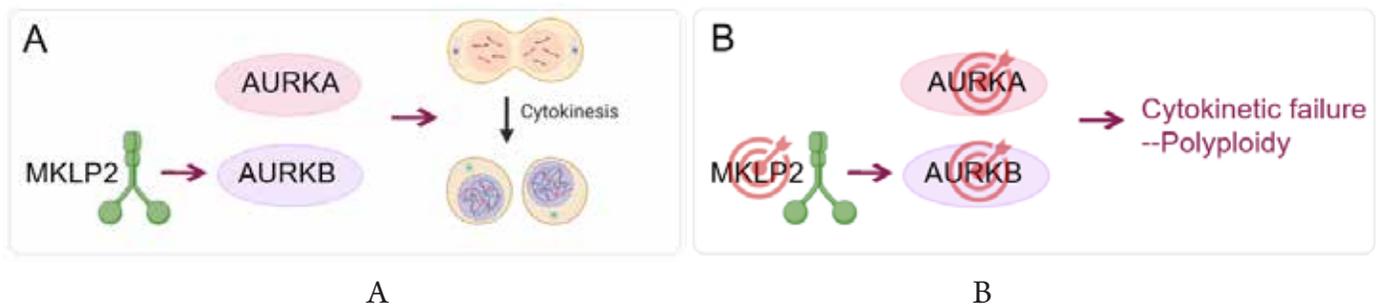


Figure 1. (A) The cell cytokinesis typically happens when MKLP2, AURKA, and AURKB are not being inhibited. (B) A strategy of leading cytokinetic failure and the accumulation of polyploids

Lead compound screening

The screening was based on 616 compounds from a molecule library, by using an In-Cell analyzer 2000 for a high throughput screening with 20 μM compound concentration. The cell used was the RPE-MYC^{H2B-GFP} cells. The results of polyploids, were available to see after 72 hours. To be more explicit, we made a diagram of the screening resulting from the total 616 compounds that were

in a same concentration (Fig. 2 A). The compact dots on the top are the inactive compounds, and the distributed dots below are the 12 compounds that could induce polyploids under their minimum effective concentration. The red dot on the bottom is the most active, which was GHG192. The cells with GHG192 showed that they have become 100% polyploidy with the drug after 72 hours.

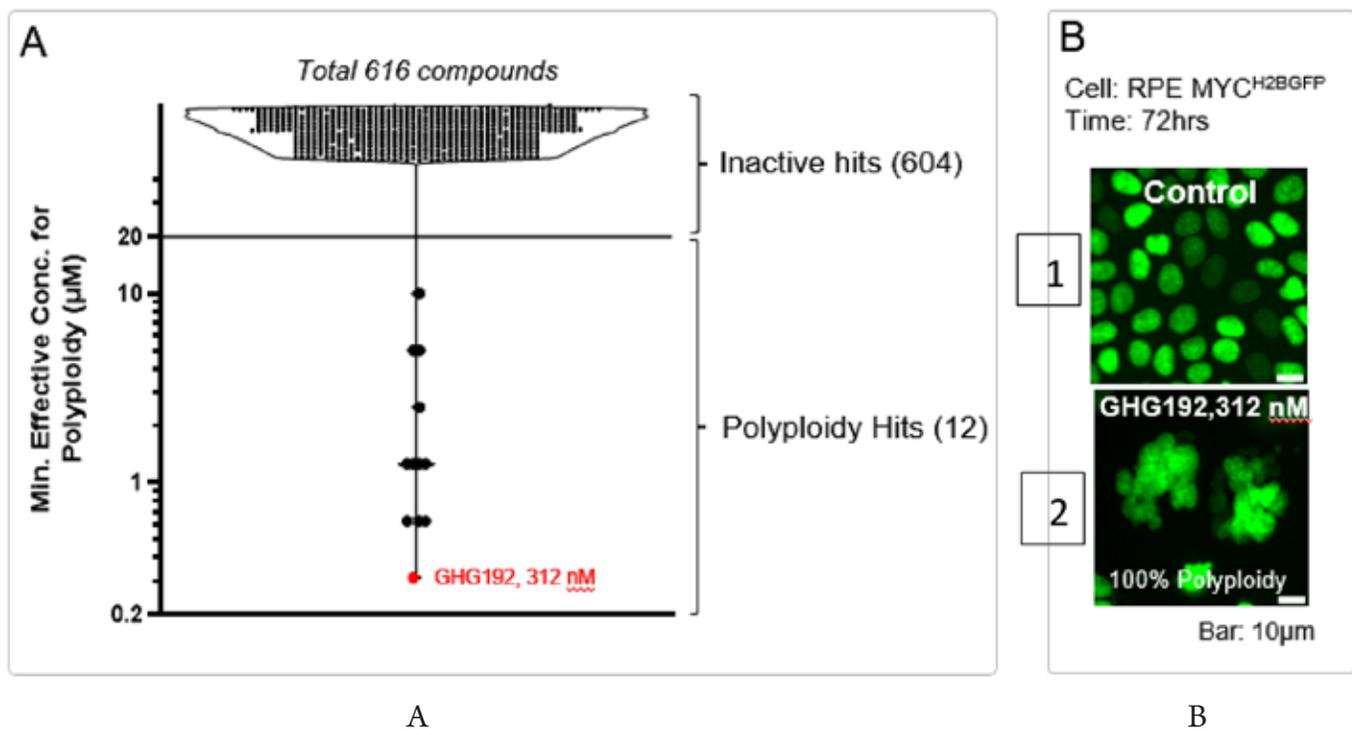


Figure 2. Screening for drugs that could induce the existence of polyploids. (A) The screening of drugs from 616 compounds from a molecule library, where one dot represents one compound. As the effective concentration for polyploidy decreases, fewer drugs can induce polyploidy, in which the only GHG192 is left in 312 nM. (B) Images of cells captured typically (Fig. 3B1) and after the inhibition of GHG192 at 72 hours (Fig. 3B2) by In-Cell analyzer 2000 and became 100% polyploidy. (Bar: 10 μm)

GHG192 inhibits AURKB, AURKA, and MKLP2 at the concentrations of polyploidy

In order to examine the reason of cytokinetic failure, we assayed for three essential mitotic regulators during cell division: AURKA, AURKB, and MKLP2. After 6 hours' drug treatment, the result was shown by IF staining.

AURKB was inhibited by GHG192 of 312 nM, 625 nM, and 1250 nM shown through phosphorylation of Ser10 at Histone 3 as AURKB's activity

(Fig. 3). Simultaneously, AURKB's activity is already being blocked at 312 nM due to the indiscernible lights, as expected in the positive compound AZD1152. The β -tubulin is used to tell the cells' cytokinesis by staining the micro-tubulin, located in the spindle, showing which are prophase and metaphase cells, as expected to be observed. Therefore, this data supports that GHG192 could inhibit AURKB.

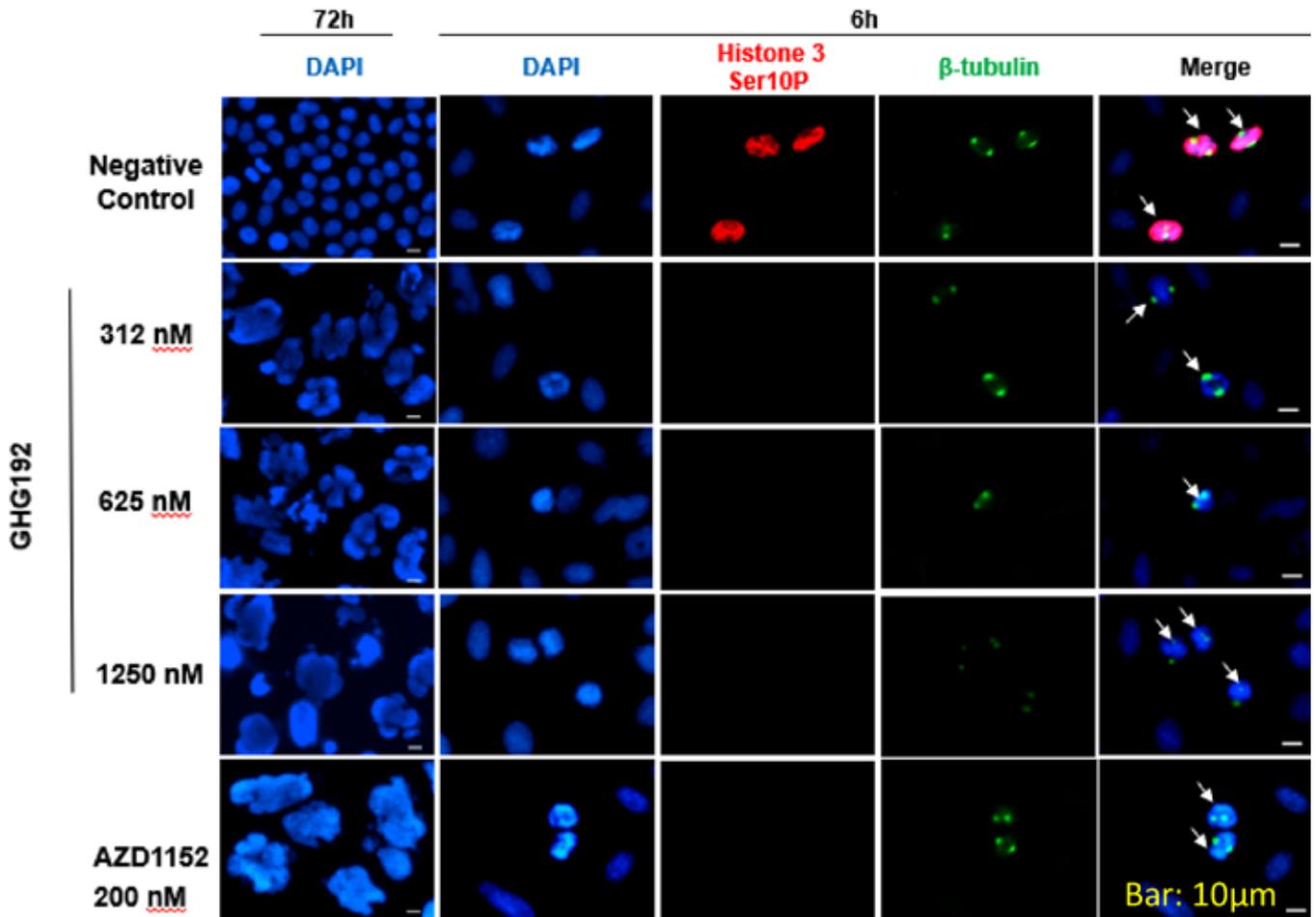


Figure 3. AURKB's activity is inhibited by GHG192. Cells were treated with the different drug concentrations for 6 hours and screened to check the phosphorylation of Ser10 at Histone 3. The first DAPI column is the polyploids formed after 72 hours (Bar: 20 μ m); while the second DAPI column represents the nuclei after 6 hours; the β -tubulin is used to stain the micro-tubulin in order to tell us the mitotic phase of cell's cytokinesis; and the AZD1152 row, as AURKB's specific inhibitor, represents the positive control. Bar: 10 μ m

MKLP2 was also inhibited by 312 nM, 625nM, and 1250 nM of GHG192. MKLP2's activity is responded to by relocating of AURKB from chromosomes to the spindle midzone during the transition from metaphase to anaphase. In other words, MKLP2 always follows the location of DNA during metaphase, and transfers to the spindle midzone during the transition to anaphase, for which MKLP2 is needed during this process. Likewise, the transition of AURKB would not occur if MKLP2 is inhibited. In the negative control group, AURKB stays in the spindle zone of the cell, which is a place between the two chromosomes. However, as the inhibition of GHG192 occurs, AURKB is already be-

ing inhibited and remains on the chromosomes of anaphase cells at 312nM (Fig.4). Hence, they agreed on the effect the inhibition of GHG192 has on MKLP2.

AURKA's activity is monitored by autophosphorylation at Thr 288 P. Similarly, AURKA was inhibited by GHG192 at 312 nM, 625 nM, 1250 nM, and they all successfully inhibited AURKA's phosphorylation as expected in the MLN 8237 row (Fig.5). Thus, this helps to prove that GHG 192 can inhibit AURKA.

In brief, the data above all strongly supports that GHG192 can inhibit the cytokinesis and the activity of AURKB, MKLP 2, and AURKA from the concentration 312 nM to 1250 nM.

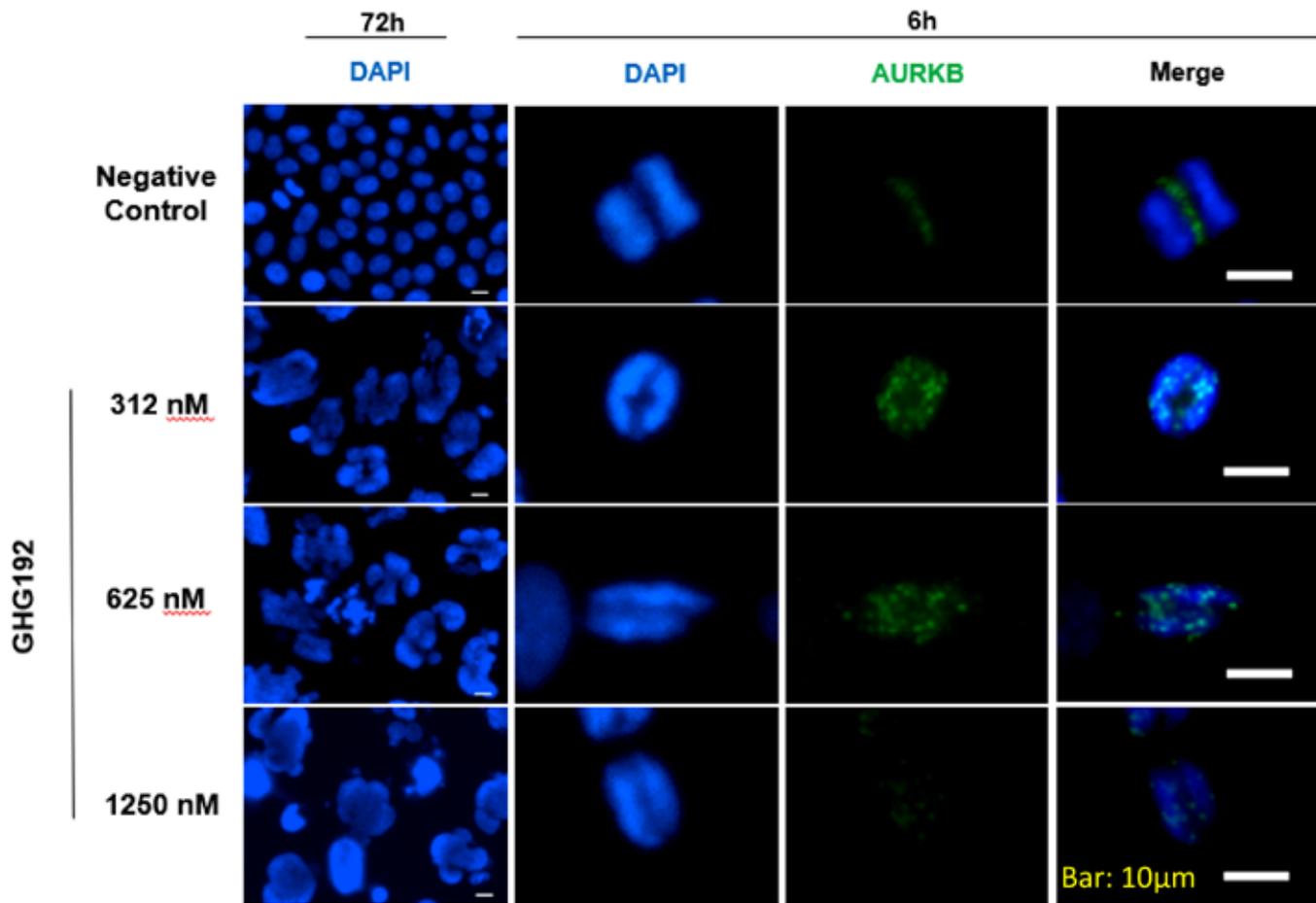


Figure 4. MKLP2's activity is inhibited by GHG192. Cells were treated with the indicated drug concentration for 6 hours and screened to read the phosphorylation at AURKB, representing its activity. The first DAPI column is the polyploids formed after 72 hours (Bar: 20µm), while the second DAPI column represents the nuclei after 6 hours. Bar: 5µm

GHG192 elicits cell death in human cancer cell lines

After we verified the effects of GHG 192 in model cells, we further explored this study in human cancer cell lines. Thus, we assayed the effect of small molecular compounds on cellular proliferation and DNA content in the same experiment. To do that, we chose NCI-H23, a lung cancer cell line; HCT116, a colon cancer cell line; Hela, a cervical cancer cell line; and DU145, a prostate cancer cell line; of which they all include high-expressions of MYC.

On the third day after the beginning of treatment, we used the MTT assay to test cell viability. According to the graphs (Fig. 6, 1–4), it is showed that as the

concentration increases, the cell viability decreases, especially in NCI-H23 (Fig. 6, 1), Hela (Fig. 6, 3), and DU145 (Fig. 6, 4). Data from the table (Table 1) was supportive through their 'Minimum Concentration for Polyploidy' column and 'LC50' column, in which the numerical values were almost the same. However, the HCT116 (Table 1) data were not as approximate as others, and the graph (Fig. 6, 2) also shows that cells barely dies as the concentration increases. Hence, we believe there might be some oncogenes in HC116 that could prevent death when forming polyploids. Together, we conclude that GHG192 simultaneously elicits cell death and induces polyploidy formation.

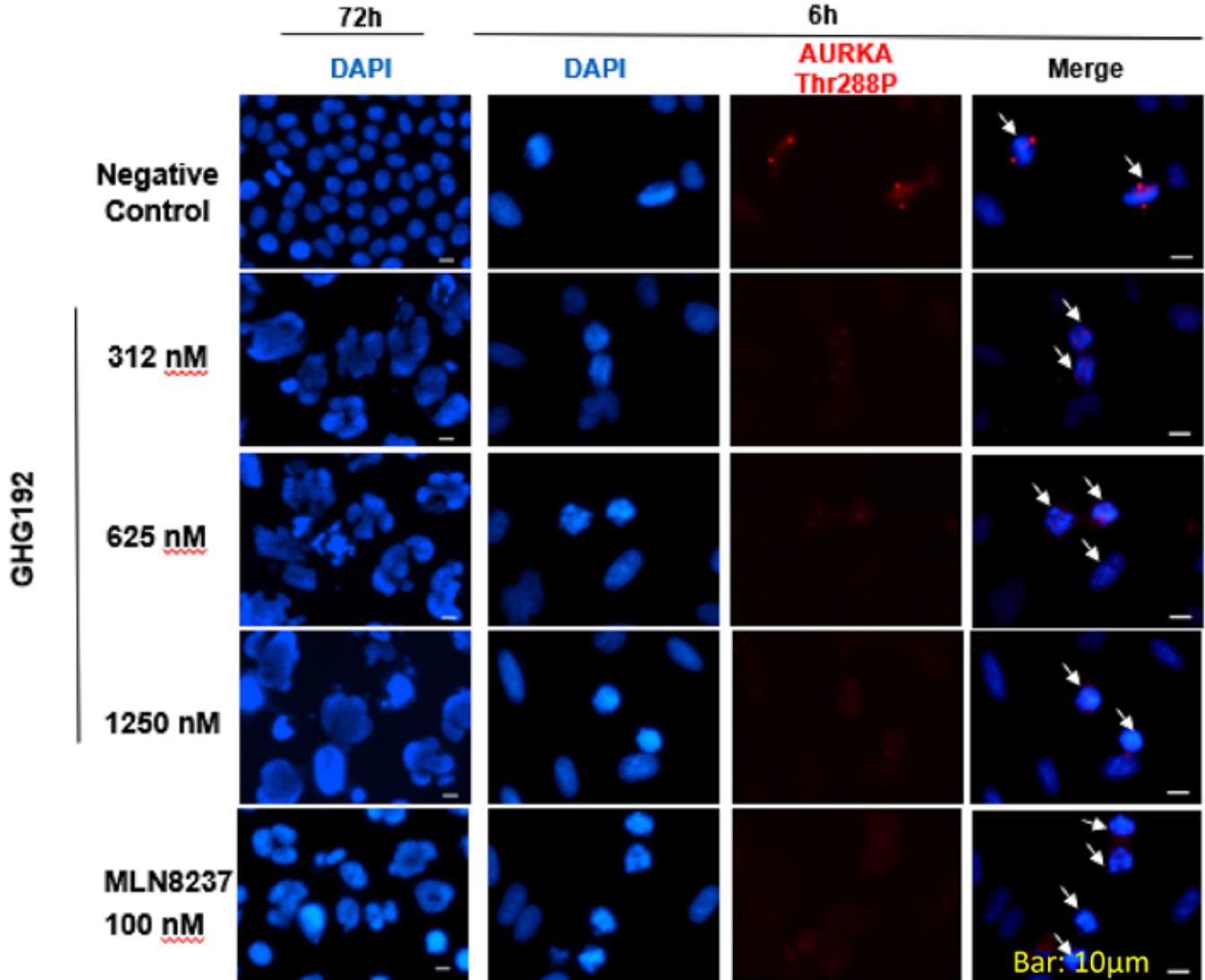


Figure 5. AURKA's activity is inhibited by GHG192. Cells were treated with the indicated drug concentration for 6 hours and screened to read the auto-phosphorylation at Thr288P, representing its activity. The first DAPI column is the polyploids formed after 72 hours, while the second DAPI column represents the nuclei after 6 hours, and the MLN8237 row, as a specific inhibitor of AURKA represents the positive control. Bar: 10µm

Conclusion:

GHG192 can elicit polyploidy and cytokinetic failure due to the inhibition of AURKA, AURKB, and MKLP2. As the most crucial part, GHG192 can elicit cell death as associated with polyploidy formation in human cancer cell lines. Although it is unknown if *in vitro*, GHG192 has an effect in more

human cancer cell lines or if other mitotic regulators could elicit polyploidy in cells; or if *in vivo*, there's efficacy and PK study in the mouse model and optimize the structure to improve the potency of compounds; GHG192 has the potential to serve cancer patients in future therapies.

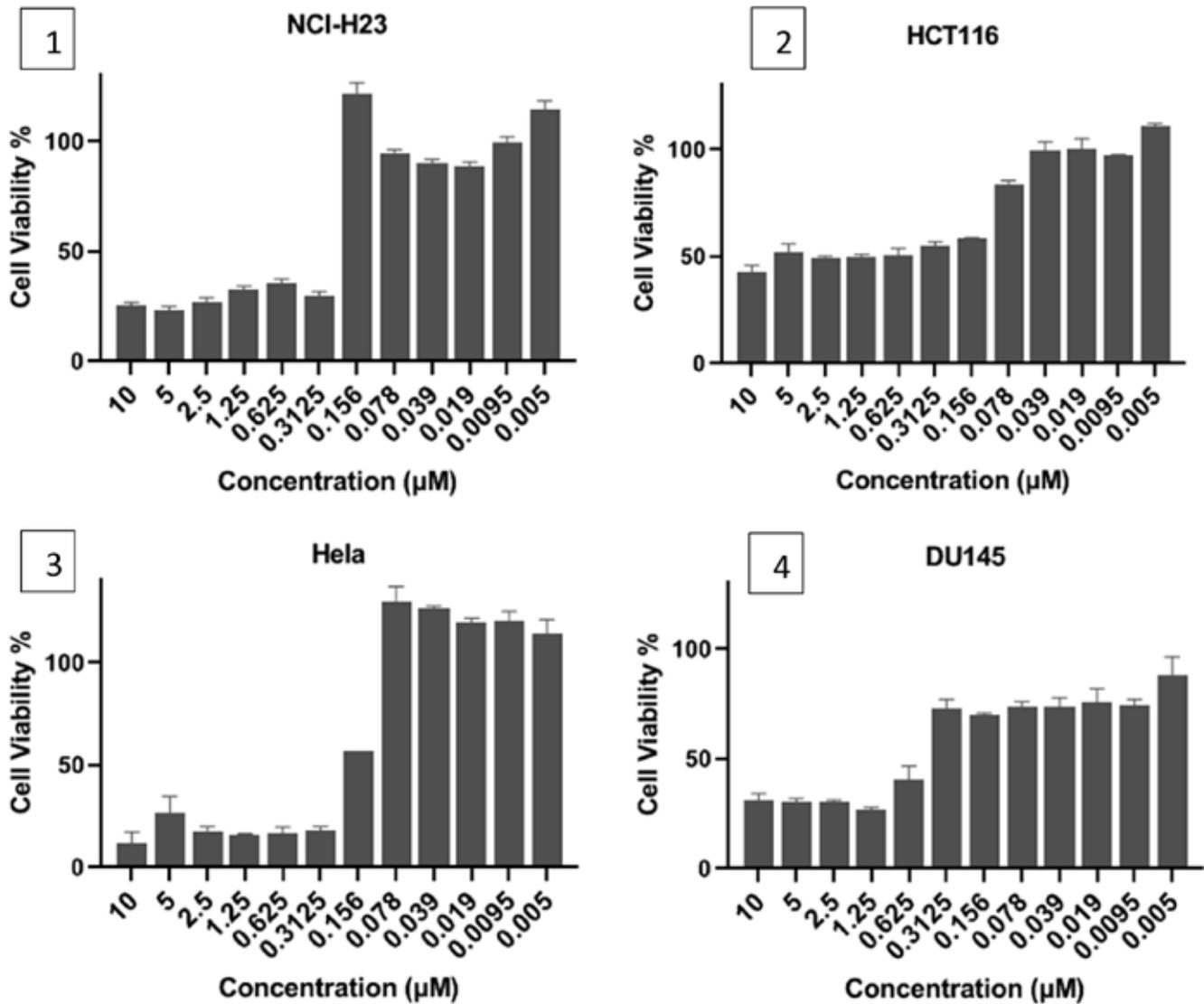


Figure 6. GHG192 elicits cell death at different concentrations. Cancer cell lines were treated with the drug for 3 days and produced data by a microplate reader. The data shown vertically are the percentages of cell viability, and the data presented horizontally are values of concentration, which is decreasing from left to right

Table 1. – The minimum concentration of GHG192 to induce polyploidy and the of concentration value lead to death when the cell viability equals to 50% (LC50). If a cancer cell' s two data are close to each other, meaning that the lethal concentration is almost the same as its minimum concentration for polyploidy

Tissue subtype	Cell lines	Min. Con. For Polyploidy (µM)	LC50 (µM) (cell viability=50%)
Lung	NCI-H23	0.312	0.2643
Colon	HCT116	0.156	0.4058
Cervix	Hela	0.156	0.1449
Prostate	DU145	0.625	0.5587

Acknowledgements:

I would like to express my biggest thank to Dr. Yang as well as other researchers for giving me the chance to work at J. Michael Bishop Institute of Cancer Research, explore the area I am interested in,

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Declaration

I, Yixuan Yun, declare that the contents of the research paper, entitled “Targeting of AURKA, AURKB, and MKLP2 by GHG192 Blocks Cytokinesis”, were obtained from the research work and results provided and guided by my supervisor, Dr. Dun Yang and Qiong, Shi at the J. Michael Bishop Institute of Cancer Research in Chengdu, China. As far as I am aware, the research paper does not include any results that have been published or written except for the references. I consent to bear all relevant responsibilities if there is anything wrong with the research paper.

Section 2. Medical science

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Venger Andrii,
PhD (biology), docent
Odessa national medical university

Venger Olga,
PhD (biology), lecturer
The state institution South Ukrainian
National Pedagogical University
named after K. D. Ushynsky

Oslavska Tetiana,
PhD (medicine), associate professor
PhD (biology), docent
The state institution South Ukrainian
National Pedagogical University
named after K. D. Ushynsky

Oslavskiyi Oleksandr,
PhD (medicine), associate professor
Oslavskiyi's dentist clinic

Vasina Yuliia,
Student, Odessa national medical university
E-mail: venger87@ukr.net

MODEL OF DIAGNOSTICS OF AMELOGENESIS IMPERFECTA IN HUMAN BY POLYMERASE CHAIN REACTION

Abstract. Method of diagnostics of amelogenesis imperfecta by polymerase chain reaction in human was created. PCRs *in silico* were conducted. Evolution history of genes associated with amelogenesis imperfecta in human by bioinformatic methods was described.

Keywords: Amelogenesis imperfecta, polymerase chain reaction, diagnostics in silico, dental disorders.

Introduction

In human enamel is synthesized during their tooth growth after birth as an extracellular matrix in a pathological process called amelogenesis. This obligate process occurs in two different stages. In

the first (secretory) stage of this process, the ameloblast produces a partially mineralized protein cluster, which will correspond to the enamel in adult tooth. In the second (maturation) stage, the protein cluster is degraded, and mineralization

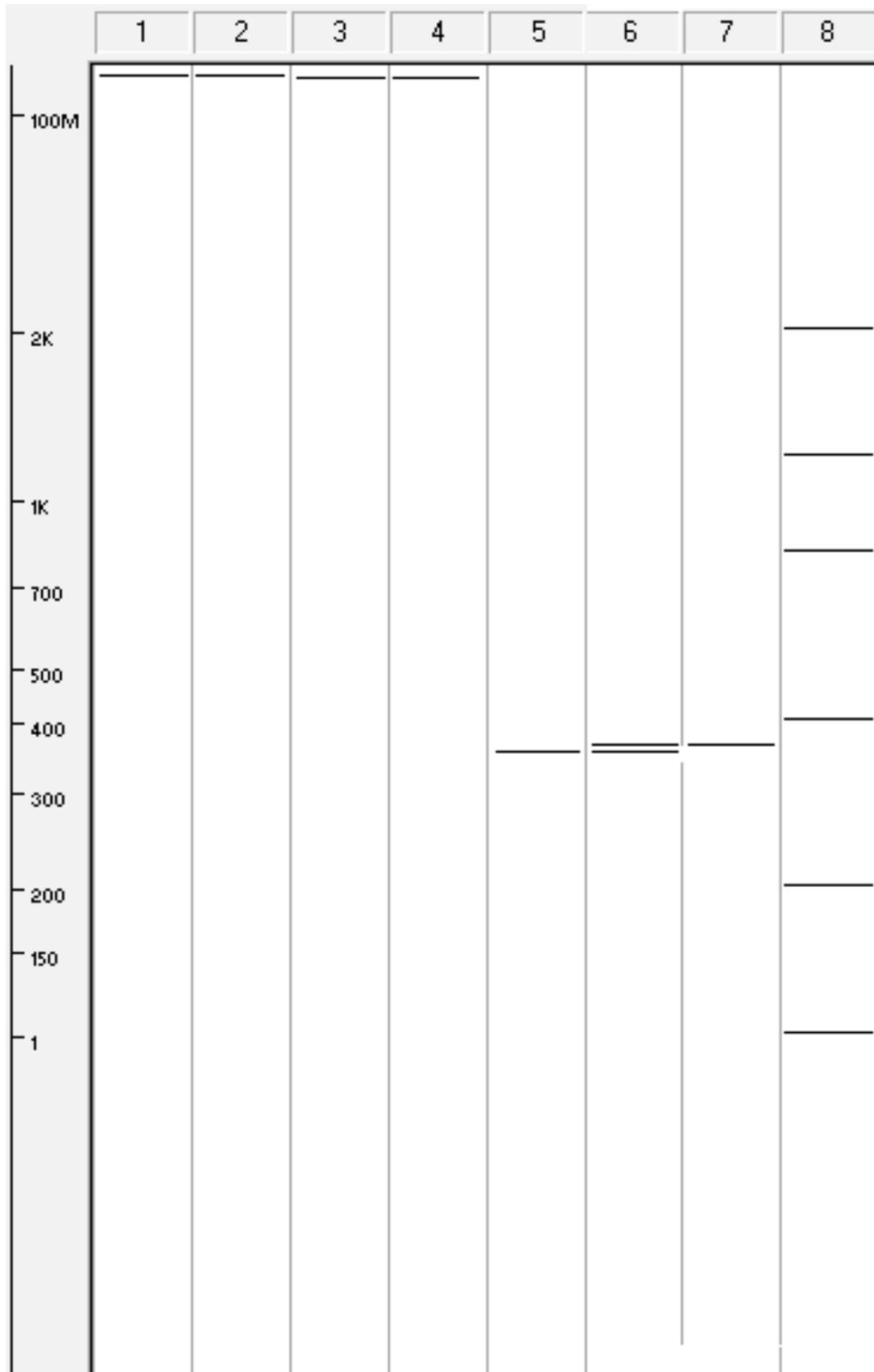


Figure 1. Products of PCR *in silico* with obtained primers and AI encoding gene.
1, 2, 3 – negative control (sequences without primers). 5 – normal homozygote form;
6 – normal heterozygote form; 7 – disorder form; 8 – marker of molecular weight Ladder 50

is completed. Amelogenesis imperfecta (AI) is a group of hereditary diseases that cause alterations in the structure and chemical combination of the enamel matrix during development [1; 2, P. 260; 5, P. 205].

Currently, the diagnosis of this disorder involves a clinical and chemical examination, and if it is possible, the diagnosis involves also structural and DNA analysis [3, P. 320; 4, P. 84].

The first AI-causing gene disorders were identified in the genes encoding the enamel matrix proteins (EMPs), known to make up the bulk of the secreted enamel organic matrix.

Their encoded proteins have a distinctive architecture of a signal peptide and a conserved casein kinase 2 phosphorylation domain likely to be targeted by family with sequence similarity 20, member C [6, P. 270; 9, P. 695; 7, P. 245].

The aim of the current work was to create PCR method of detection of AI disorder forms and to conduct PCRs *in silico* by bioinformatic methods.

Material and methods

Polymorphism of AI encoding gene of *human* was researched by polymerase chain reaction (PCR) *in silico*. Primers and time-temperature environment for PCR were chosen by VectorNTI10 program.

120 nucleotide sequences of normal and 68 disorder forms of AI encoding gene from National Centre of Biotechnology Information were analysed by PCR *in silico* with Fast-PCR program [10].

The evolutionary history of AI encoding gene was inferred using the Neighbor-Joining method. Evolutionary analyses were conducted in MEGA6 [8, P. 1238].

Results

By VectorNTI10 program for analysis of polymorphism of AI encoding gene of human there were created the following primers (5'–>3'): EMP-FACAAACAAATGGCGGCATCG and EMPRGGGGTACTGTTTCCTGTGGG.

Condition of PCR was: 2 min at 94 °C for first denaturation; 35 basic cycles of 0,5 min at 94 °C, 1 min at 54 °C, 1,5 min at 72 °C; and 10 min at 72 °C for final elongation.

Results of PCR analysis are present in (table 1).

Table 1.– Products of PCR analysis *in silico*

Forms of allele	Products of PCR, base pairs		
	353, 353	353, 355	355, 355
Number of samples			
Normal forms	64	56	–
Disorder forms	–	–	68

Discussion

The most popular combination of products of amplification *in silico* was 355, 355 base pairs (bp). Normal forms contained 353, 353 and 353, 355 bp. Disorder forms were 355,355 bp only. It means that disorder form is homozygote and allele of disorder (AI) is recessive.

Results of PCR *in silico* with the obtained primers and sequences of AI encoding gene are present in the (Figure 1).

The optimal tree of detected sequences with the sum of branch length = 8.28086334 is shown. The percentage of replicate trees in which the associated taxa clustered together in the bootstrap test (500 replicates) are shown next to the branches. The tree is drawn to scale, with branch lengths in the same units as those of the evolutionary distances used to infer the phylogenetic tree. The evolutionary distances were computed using the Poisson correction method and are in the units of the number of amino acid substitutions per site. The analysis involved 8 amino acid sequences. All positions containing gaps and missing data were eliminated. There were a total of 138 positions in the final dataset.

Results of analysis of evolutionary history of AI encoding gene are present in the (figure 2).

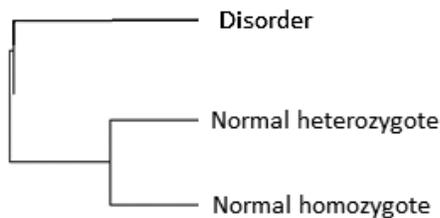


Figure 2. Evolutionary history of AI encoding gene in human

Conclusion

In result of the accomplished research the evolution history and the primers and conditions of PCR for detection of polymorphism of AI encoding gene of human were created and conducted. Unique combination of alleles of disorder forms of AI was described.

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Mingyue (Cynthia) Jia,
12th grade, Worcester Academy,
Worcester, Massachusetts, United States,
E-mail: Mingyue.jia@worcesteracademy.org
Dr. YingQin Taylor,
Instructor
E-mail: yi213@outlook.com

MACHINE LEARNING IDENTIFYING THE RELATIONSHIP BETWEEN THE FIELD OF HOSPITAL INVESTMENTS AND THE LENGTH OF HOSPITAL STAY

Abstract. The objectives of this research are to investigate the impact of hospital amenities on the length of hospital stay using a machine learning model and set up a priority list for the distribution of funds in each field to increase hospital efficiency. I hypothesize that all technology innovations like the MRI units in healthcare will have an impact on the length of the hospital stay. Therefore, investing the greatest proportion of funds on MRI units among all potential factors that impact the length of the hospital stay will give the strongest and direct return to the healthcare system efficiency. Through data analysis, all variables appear to affect the hospital stay, which is further confirmed in the linear regression model. The linear regression model was trained to explore the relationship with 91.76 accuracies and 0.87 r^2 values. The coefficient revealed that, among variables, both positive and negative effects on the length of the hospital stays exist. However, the only controllable negative impact on the hospital stay was on the number of MRI units which had the coefficient of -0.90 , meaning that if more MRI units are invested by the hospital, the shorter the hospital stay. It directly presented an example of hospital innovation making the healthcare system more efficient and effective. From there, my hypothesis was proven correct. The established list of priorities for funds distribution for increasing healthcare efficiency could also be used in future decisions in healthcare investments.

Keywords: Hospital stay (care intensity), healthcare investment, healthcare innovation, machine learning model, linear regression.

Sickness, injury, and death are the inevitable factors in the course of every human's life. The healthcare system, therefore, was invented to provide and maintain effective medical protection and care. Especially after the Covid-19 pandemic, the different pandemic responses around the globe had underscored the power of a strong and effective healthcare system to the community. Meanwhile, people had also witnessed the consequences of inadequate investment

in healthcare equipment like the lack of hospital beds, ventilators, and advanced diagnostic techniques, leading to an increased length of hospital stay that further intensifies the problem. In this case, it is highly important for the hospital administrators to determine how they should distribute their limited funds in their hospitals. To explore more on this task, this study focuses on two steps: first, determining the impact of five hospital factors – Time (years), Types of healthcare policy, Hospital beds, MRI units, and

in healthcare equipment like the lack of hospital beds, ventilators, and advanced diagnostic techniques, leading to an increased length of hospital stay that further intensifies the problem. In this case, it is highly important for the hospital administrators to determine how they should distribute their limited funds in their hospitals. To explore more on this task, this study focuses on two steps: first, determining the impact of five hospital factors – Time (years), Types of healthcare policy, Hospital beds, MRI units, and

CT scanners – on the length of hospital stay. Then, I focus on setting up a priority list for the amount of funds to be invested in each field.

1.1 Background Information

Hospital stay is defined as the time a patient using a hospital bed stays on one hospital site during a hospital provider spell (NHS). The longer the length of a hospital stay usually indicates the greater intensity of the illness, the low quality of the medical care received, and the insufficient healthcare coverage. Although there are exceptions in interpreting the hospital stay, people still believe that the length of the hospital stay can be a representative factor that reflects the healthcare system's efficiency.

Hospital Beds are defined as the number of beds provided by the hospital to support patients with the needs of hospital stay. An increased number of hospital beds in a hospital means a greater capability for that institution to treat more patients and provide more throughout care.

The CT (Computed tomography) scanner is an x-ray machine that combines many x-rays images to create cross-sectional views and three-dimensional images of the patient's internal body structures and organs. It is hospital equipment in helping diagnose a range of conditions

(OECD). The MRI (Magnetic resonance imaging) facilitates the diagnosis of the patients by visualizing the internal structure of the body like brain, chest, and abdomen. It functions based on magnetic and electromagnetic fields. The magnetic fields induce a resonance effect of the hydrogen atoms, creating electromagnetic emissions. Then, the emissions are further registered and processed by computers, producing images of the body structures. Unlike conventional radiography and CT scanning, MRI exams do not expose patients to ionizing radiation. Therefore, a greater number of CT scanners and MRI units will increase the efficiency of the diagnostic process, further boosting the quality of the healthcare system (OECD).

The healthcare model in the current society includes three major parts, the provider (hospital),

the patient, and the third-party payers (insurance company, government, and employers). The patient seeks care from the provider with the money being covered by the payers through the healthcare policies that the patient signed up with. Although the idea of a healthcare system seems universal, each country still has its healthcare policies. In the United States, the majority of Americans are under the policy from private insurance companies. The coverage is non-universal, meaning only a portion of the expenses will be paid by the third-party payer. On the other hand, Australia offers a universal healthcare system called Medicare, which is the primary form of access to healthcare in the country. It covers 100% of the expenses for the care within state-funded hospitals. The difference between the amount of money covered by the different policies may have a direct impact on the length of the hospital stay; that is, sufficient coverage of a healthcare policy will increase the hospital stays since the out-of-pocket payment is reduced.

1.2 Special Approach: Machine Learning

Machine learning is defined as a study of computer algorithms that gives "computers the ability to learn without being explicitly programmed". (Arthur Samuel, 1959). In some cases, the machine learning model can be understood as the computer file that is trained by a set of data and provided with algorithms that can reason and learn from those data to recognize a certain pattern and improve (Microsoft). With a huge data entry and knowing that different variables have a complex impact on the hospital stay when influencing each other, an efficient and flexible way of analyzing the data is essential. To this end, I decided to train a linear regression model that will first learn from the discovered pattern and further predict the overall length of the hospital stay under all five variables.

2. Method and Basic Data Analysis

2.1 Data Gathering

All data used in this study are from the Organisation for Economic Co-operation and Develop-

ment (OECD) website. The OECD is an international organization that focuses on building better policies for better lives. It provides a unique forum for data and analysis, exchange of experiences, best-practice sharing, and advice on public policies and international standard-setting (OECD). The countries that participated in the organizations include Australia, the United Kingdom, countries in central Europe, United States, South Korea, Japan, etc.

The first part of the data was released in 2020, with 6 variables (5 responsive and 1 dependent), 518 entries, and no missing value. It contains 32 non-repeated countries, but each country has different numbers of values, depending on the year of data collection. All variables were kept since we hypothesized that all 5 different responsive variables have a relationship with the length of the hospital stay. While analyzing the data, I found out that all the data

under hospital beds are the same value for the MRI units. In this case, I removed the hospital beds variable in the first part of the data and looked up a new data set for hospitals beds.

The second part of the data was also from the OECD website and released in 2020, with 3 variables, 14994 entries, and no missing value. It contains 32 non-repeated countries, while each country has different numbers of values, depending on the years of data collection. Only the entries that describe the total hospital beds were kept. Because the new data set has a different naming format for countries, I used the `pycountry` function in python to abbreviate the name into 3 letters, as displayed in the first part of the data.

Finally, I merged two separated data sets into one single data table by using the `pd.merge` function. The first 10 entries are shown below in (table 1):

Table 1.– First 10 Entries of Dataset

No.	Country	Time	Average Hospital stay (days)	# of MRI units (per million population)	# of CT scanners (per million population)	# of Hospital beds
1.	Aus	1992	6.6	1.43	16.71	81255
2.	Aus	1994	6.4	2.36	18.48	81643
3.	Aus	1995	6.5	2.89	20.55	82477
4.	Aus	1996	6.4	2.96	21.95	79802
5.	Aus	1997	6.2	3.53	23.34	78828
6.	Aus	1998	6.1	4.51	24.81	77631
7.	Aus	1999	6.2	6.01	25.52	76612
8.	Aus	2000	6.1	3.52	26.28	76875
9.	Aus	2001	6.2	3.79	29.05	76209
10.	Aus	2002	6.2	3.74	34.37	76653

2.2 Descriptive Data Analysis

Descriptive data analysis was used as the first step of data analysis in this research. It summarizes and describes the data through descriptive statistics (Neo 2020).

2.2.1 Count Plot

In figure 1, the count plot reflects the total counts of entries recorded under each country. The counts

of entries were set descending. Knowing different entries corresponded to different years, the maximum number of entries in this count plot reflected that there are 25 years of data recorded in Russia and Finland and there are less than 5 years of data recorded in Portugal.

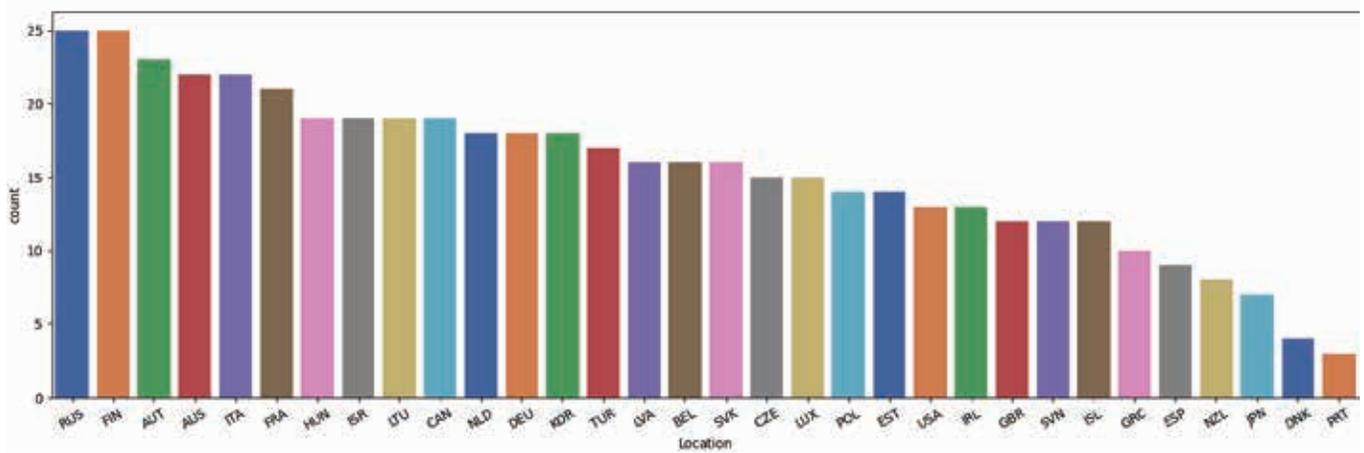


Figure 1. Count Plots of Entries in Different OECD Countries

2.2.2 Histogram of Variable Distributions

Other than looking at the distribution of data counts, I also generated five histogram plots that

show the distribution of data values under each different variable, as shown in (figure 2).

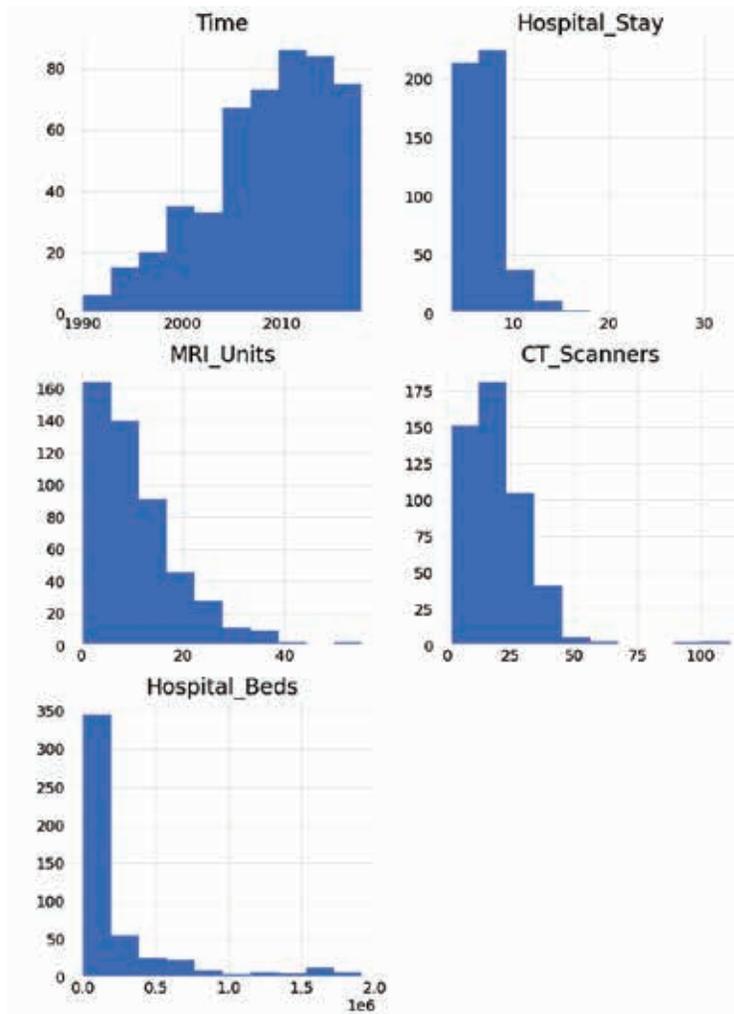


Figure 2. Histogram of Variable Distributions

Depending on different types of values, each histogram has its unique dependent variable with different units. The hospital beds reflect the total beds count, whereas the MRI_units and CT_scanner are in the unit of per million people. The hospital stay is in the unit of days. The time histogram is skewed to the left, meaning the majority of data were collected in the recent years between 2010 and 2020. The histogram also indicates that the length of the hospital stays is generally between 0 to 10 days with few exceptions.

2.3 Exploratory Data Analysis

The second data analysis process is the exploratory data analysis (EDA). Its goal is to explore the data and find the previously unknown relationships between variables through graphs and statistical summaries (Neo 2020). To generate such graphical visualizations in python, I used python interpreters pandas, numpy, matplotlib, and seaborn.

2.3.1 Heat Map of Variable Correlations

The first step of the EDA was creating the heat map of variable correlations to find out the correlation between two variables.

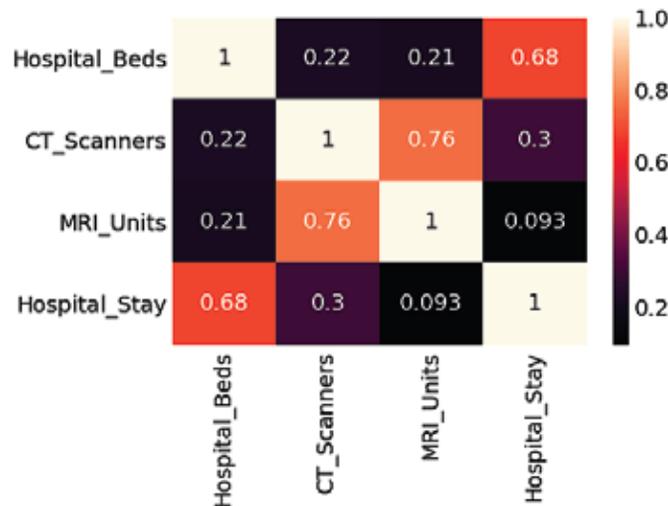


Figure 3. Heat Map of Variable Correlations

As shown in figure 3, the final heat map includes four different components: four variables in both x and y-axis, the correlation R values between -1 and 1 , and the color-coded index for different R values. The correlation R measures the direction and strength of the graph. Its value is between -1 (strong negative correlation), and 1 (strong positive correlation). When the R-value is close to 0 , it indicates that there is no correlation between the two variables. According to figure 3, all the values are positive, meaning that there is no negative correlation involved. The color-coded from 1.0 to 0.2 , the darker the color the closer the value to 0 , meaning there are less likely to have an established correlation.

The MRI_unit and the CT_scanner have the highest R-value 0.76 . Although 0.76 is very close to 1 , we still can't fully accept that they have a posi-

tive correlation. However, the value does indicate a potential relationship between the MRI_unit and the CT_scanner. When creating a machine learning model, a strong correlation needs to be avoided. This is because the stronger correlation makes changing the variable independently very difficult since they tend to change in unison, leading the accuracy of model estimating relationships to decrease. Since no strong correlation is discovered in the graph, no two variables need to be used together when building the model (Valentin Calomme, 2017).

2.3.2 Aggregation by Location Plot

To analyze the relationship between each variable to the total hospital stay, I created a line graph with average hospital stay aggregated by location as Figure 5 below.

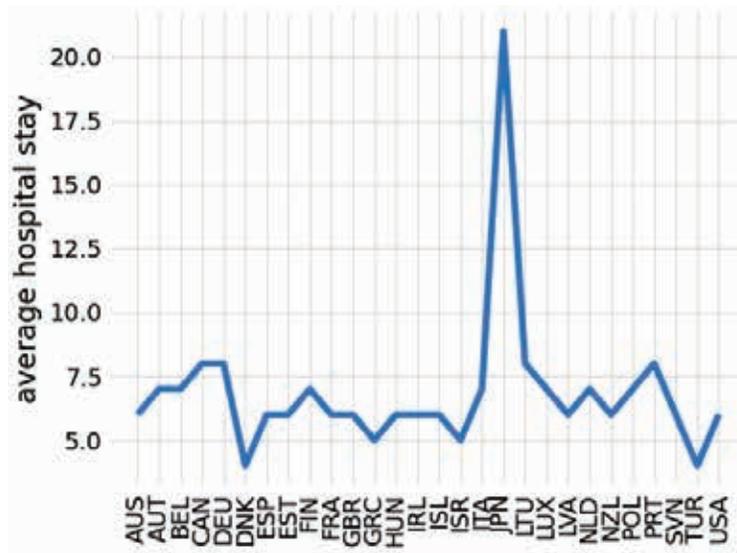


Figure 5. Aggregation by Location Plot

The figure 5 shows the average hospital stay aggregated by locations. The length of the hospital stay was averaged by the total data counts of each country. As the plot displayed, the range of the average hospital stays is about $21.5 - 0.4 = 21.1$ days. However, if the average hospital stay from Japan (JPN) is removed, the range of the hospital stays will be much smaller, becoming roughly $8.0 - 0.4 = 7.6$ days. In this case, the plot shows that Japan could be a potential outlier in the hospital stay data. The reasons for Japan’s high hospital stays are their huge number of the aging population and the insurance coverage. Japan’s aging population is always at the highest among all other countries, which

may lead them to a great number of healthcare needs and treatments. Their healthcare policy can also be a factor. With a great amount of money being paid by the third party, fewer people would be forced to leave the hospital beds due to the fact of unwillingness to conduct the out-of-pocket payment. Therefore, each country’s specific situation can have an impact on the hospital stay.

2.3.3 Box Plot for Outliers

To confirm that the average hospital stays in Japan is an outlier and to find other outliers, I used the “sns. Boxplot” function in python to create 5 box plots for different variables.

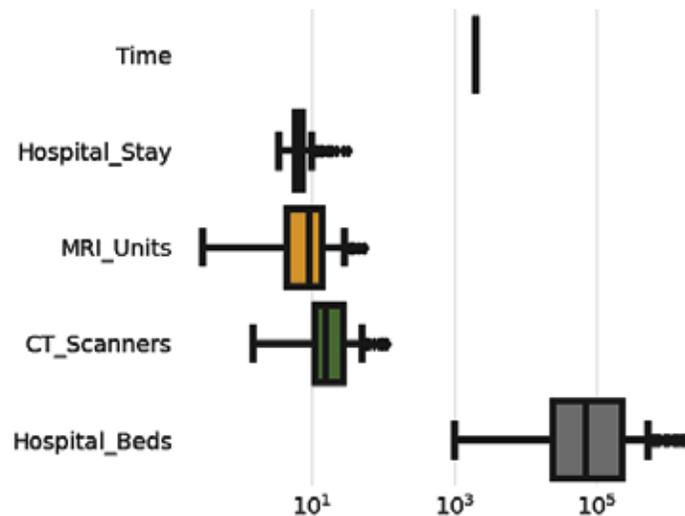


Figure 6. Box Plots of Different Variables

A box plot indicates the median, maximum, and minimum values of the data, while also showing the outlier in the form of scattered dots after the maximum bar. According to the graph, both hospital stay, MRI unit, CT scanners, and hospital beds have the potential outliers. One obvious outlier is in the hospital stay variable, which can be attributed to the hospital stays in Japan.

2.3.4 Line Graph of U.S., UK, Australia Average Hospital Stay

When first conducting the analysis, I compared the change in hospital stay between the U.S., UK, Australia, and Japan. However, since Japan appears an outlier to the data, I decided to remove Japan from the graph.

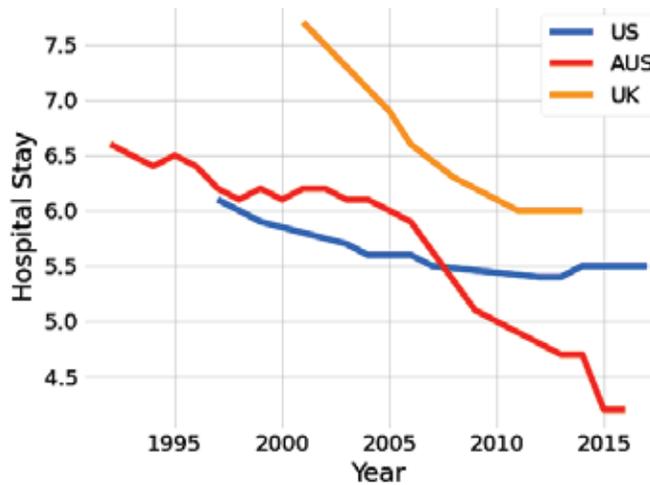


Figure 7. Hospital Stay between the US, UK, and Australia

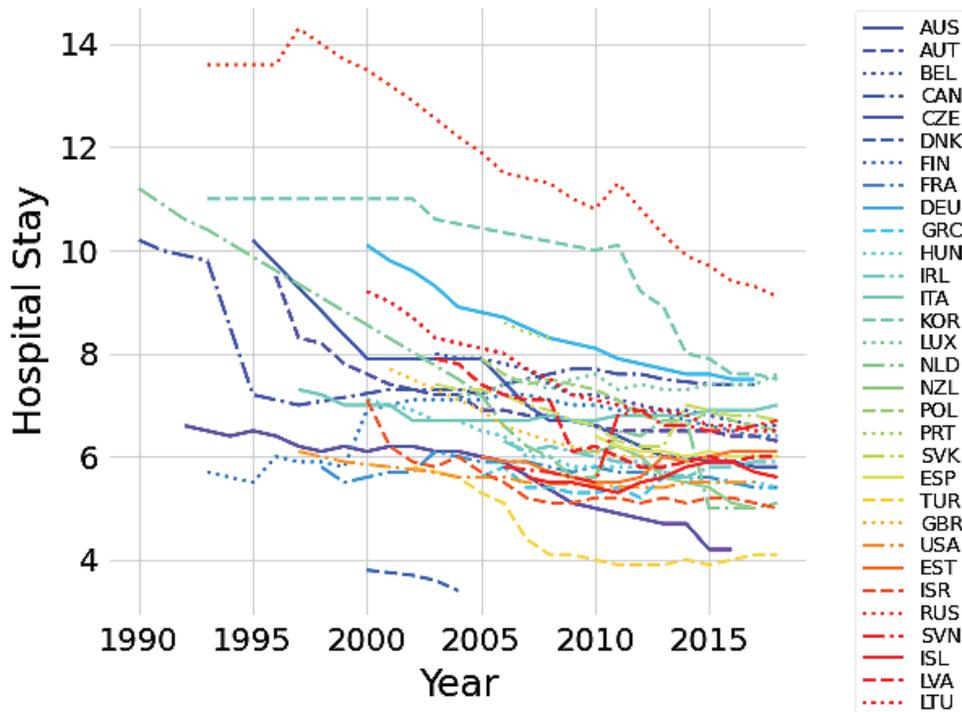


Figure 6: Line Graph of Hospital Stay in All Country without Outlier

According to figure 7, both hospital stays in these three countries decreased over time. Among all the

countries, Australia experienced the biggest decrease between 2006 to 2013, becoming the country with

the shortest length of hospital stay after 2007. Unlike Australia who has a continuously decreasing length of hospital stay, the U.S. hospital stays increased by 0.1 in the year 2013 and the UK hospital maintained the same after 2011.

2.3.5 Line Graph of All Countries Hospital Stay Over Years Without Outlier

Figure 6 shows the comparison of hospital stays over time among all the OECD countries except Japan, which was considered as an outlier. From the graph, one discovery is that the trend of hospital stay decreased over time in most countries. This can be caused by the improvement of technology. Increasing the quality of treatments and diagnostic abilities, the length of the hospital stay can be greatly reduced.

2.3.6 Aggregation by Time Plot

To further analyze the data, two plots about average hospital stay and average amenities for MRI, CT, and hospital beds aggregated by the time were created as shown in (figure 6 and figure 7).

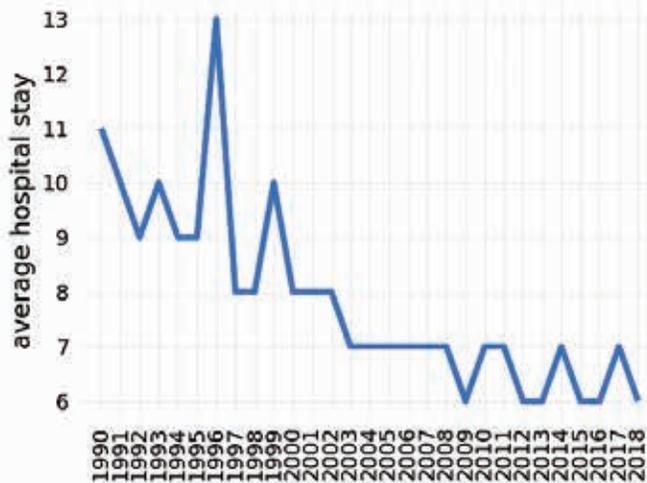


Figure 7: Average Hospital Stay Aggregation by Time Plot

Figure 7 shows that the average hospital stay is decreasing over time with two abrupt increases in 1996 and 1999. In 1996, the average hospital reached its peak of 13 days.

In (figure 8), the amenities of MRI_unit, CT_scanner, and hospital beds were averaged. Since the number of hospital beds is in a different unit than

the other variables, I re-scaled the data values with the x.scale function. As it showed in the graph, the number of hospital beds increased abruptly from 1992 to 1994. After 1994, the average amenities of the hospital beds fluctuated and reached its peak in 1999 for about 70 units of amenities. The average amenities continued to decrease after 1999.

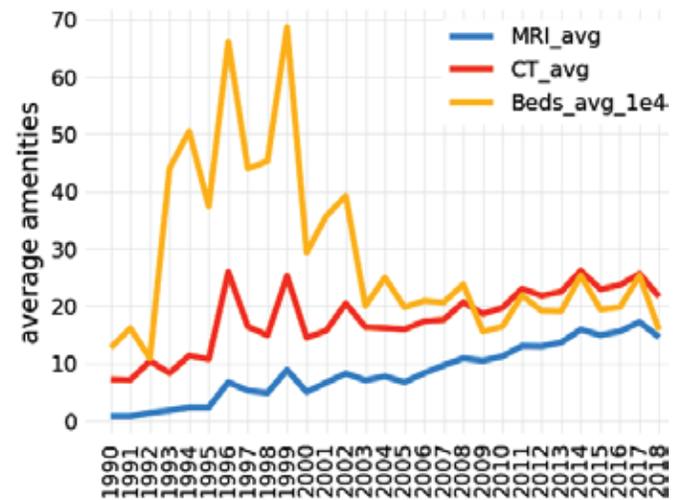


Figure 8. Average Amenities Aggregation by Time Plot

Unlike hospital beds that fluctuate over time, the average amenities of the MRI units and the CT_scanner keep increasing over time. It increased the most between 1995 to 2002. One interesting thing about the CT scanner and the MRI unit is that they increased at a similar rate every year, resulting in a similar graph. This can be attributed to the fact that hospitals often buy the MRI unit and the CT scanner together since they have similar functions but everyone has their unique specialty in diagnosis.

2.4 Data Preprocessing

With sufficient data analysis, the first step for building the machine learning model, data preprocessing, can be conducted. Function Scikit-learn is installed to preprocess the model. Before training the model, I defined the x as all the independent variables: CT_scanner, MRI_unit, Hospital beds, Times, and Locations, and y as the only dependent variables that the study was looking for: the length of the hospital stay.

Training a machine learning model highly relies on standardized variables, because a higher magnitude of the variable will be greatly focused by the model. In this case, variables with a small data magnitude will be overlooked in the learning process, leading to inaccuracy and data leakage. In this research the data magnitude for total hospital

beds has a much higher scale than that of the others, so I used the MinMax scaler function to turn all the data scales the same. Then I randomly assigned 70% of the data into the training group and 30% of the data into the testing group to teach the machine learning model. The diagram below explains the training process:

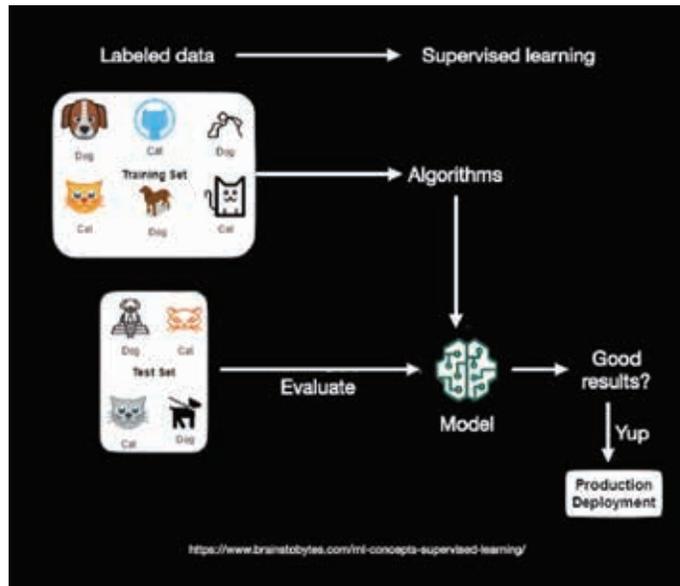


Diagram 9.

The 70% assigned data represented by the training set of cats and dogs were put into the algorithms and introduced to the machine learning model. In the meantime, the 30% assigned different data, as the test set in the diagram, were used to evaluate the model's effectiveness. Directly from their name "test", the testing set allows the x values to be inputted into the model and compare the y-predicted with y-tested. After running the process multiple times with good results obtained, a well-trained machine learning model will then be used.

2.5 Regression Model

The machine learning model used in this research is the linear regression model. It shows the relationship between x (independent variables) and y (the length of hospital stay) in a linear line. The line will help the model to predict the final y value with any different x values. Since many variables were included in the x variables, a formula for this linear model is shown below:

The coefficient in front of the x variables represent their relationship to the total predicted y (length of hospital stay). The greater the coefficient magnitude, the greater the relationship to the hospital stay. The classifier score in the program corresponds to the r^2 value that measures the percent reduction in the sum of squared residuals when using the least-square regression line to make predictions rather than the mean value of the length of hospital stay. The model also measures the mean absolute error which is the mean difference between a predicted length of hospital stay and the actual hospital stay in the test set.

3. Result and Discussion

3.1 Linear Regression Result Tables

The result of the created linear regression model is shown in (table 2) and (table 3) below.

The classifier score indicates that About 87% of the variability in the length of hospital stay is accounted

for by the least-squares regression line with $x =$ Time, MRI unit, CT scanner, Country, and Hospital beds. Since about 87% of the variability is explained by the

regression model with only 0.6 mean error and 91.76 accuracies, the linear regression model can indeed predict the hospital stays with given x variables.

Table 2. – Linear Regression Line Result

Classifier score	Classifier intercept	Mean absolute error	Accuracy
0.87	(5.446, 0.809)	0.6	91.76

Table 3. – Coefficient Result

Time	MRI_unit	CT_scanner	Country	Hospital_beds
- 2.52	- 0.90	0.29	0.56	18.36

After confirming the model effectiveness, the coefficient in front of the x variables can also be explored. Among five different variables, hospital beds have the greatest positive relationship to the length of the hospital stay. It means that if more beds were added to the hospital, the length of the hospital stay would increase. This makes sense, the more hospital beds reduce the demand, allowing people who need the bed to stay longer until recovery. Following hospital beds, the Time has the strongest negative relationship to the hospital stay. This can be caused by the improvement of technology and a better health care system, allowing people to live longer with fewer diseases and illnesses. Therefore, the negative relationship between the MRI unit and the hospital stay can also be explained by the development of technology. As a new development, the MIR scanner can take images of any part of the body in different directions. The image provided by the MRI unit is better than that of the CT scanner which differentiates the fat, water, muscle, and other soft tissues, leading the diagnostic process to be more efficient (FDA). On the other hand, the CT scanner that serves as the traditional diagnostic machine has less ability to diagnose. Therefore, even CT still facilitates the healthcare system efficiency, investing too much money on that will lead to an increased hospital stay, indicating a less efficient system.

4. Conclusion

In this research, a linear regression machine learning model is trained to determine the factor that can affect the length of the hospital stay the most among Time, MRI unit, CT scanner, Country, and Hospital beds. The linear regression model showed that every variable has an impact on the length of the hospital stay. Although hospital stay can be decreased and increased by all five variables, technological development still improves healthcare efficiency in its ways. Among all controllable variables, the MRI unit has the greatest negative relationship with a coefficient of -0.90 . Therefore, the most amount of money should be invested in the MRI unit that reduces the length of the hospital stay, increasing the healthcare efficiency and providing better care for patients. According to the result, as the bigger proportion of the fund is being distributed to the MRI unit, other research and technological developments can be the next target for hospital investment. Hospital beds also have a field to invest in. Although it doesn't decrease the length of the hospital stay, the number of beds can increase the healthcare quality since fewer people would be forced to leave hospital care due to limited capacity, which is also related to building up better healthcare policies. Investment in CT scanners should be considered last.

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Section 3. Psychology

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*Shuyang Wei,
People's Affiliated Middle School of China
E-mail:*

SMARTPHONES AND MENTAL HEALTH

Abstract. In this study, the goals are to testify the relationship between smartphone addiction and depression, smartphone addiction and anxiety, and media use and sleep respectively. In order to test the correlation, we selected variables from a secondary dataset. Specifically, we looked at the variables: sleep, depression, smartphone addiction, anxiety, media use, and general media use. In the original study participants of this study were recruited through a voluntary subject pool sign up. We found that smartphone addiction is positively correlated with depression and anxiety. However, we did not find a relationship between media use and sleep. The findings help people get a deeper understanding on how the use of smartphones relates to people's mental health.

Keywords: smartphone, media use, mental health, sleep habits, psychological well-being.

Learning efficiency

The effects of smartphone use by college students on their perceived academic performance can not be ignored. Using five hypotheses derived from the literature related to smartphone use, scientists try to reveal the relationships among variables regarding college students' smartphone use in the academic setting. Furthermore, multiple group analyses were additionally conducted to verify whether students exhibited different relationships in the hypothesized model depending on their majors. The results showed that the result is statistically significant, which indicated that all five hypotheses are correct (Han S. & Yi Y.J., [3]).

In a different study, researchers presented an interactive learning system, and they used a method of acquiring the study records for improving the students' motivation for learning. During the lecture, the students use the smartphone for learning.

They carried experiments during real lectures at the intermediate level. The results showed that the proposed study record system can improve the degree of self-learning after the lecture. The conclusion is that students should study by themselves the learning materials through the support of smartphones (Yamamoto N. & Wakahara T., [14]).

A study reviewed and synthesized recent literature relating to factual knowledge acquisition and retention and to explore its applications to medical education, which is by applying smartphones (Yeh D. D. & Park Y. S., [15]). Learning basic facts is often overlooked and underestimated in medical education. through learning the rudimentary things, distributing, or spacing, practice is superior to massed practice. Testing, compared to re-study, produces better learning and knowledge retention, especially if tested as short answers format rather than multiple choice format. Feedback is important to solidify the testing

effect. This experiment discusses the implications of applying these concepts to smartphones. Most medical trainees have smartphones, which can greatly enhance factual knowledge.

Depression

Researchers found that there are more people becoming problematic or addicted to smartphones nowadays, and they are characterized by excessive time spent on the cell phone, interference with social relationships and responsibilities, and difficulty disengaging from cell phones. The researchers believe that depression, anxiety and self-regulation may be the result of factors related to questionable phone use. The current study investigated factors during late adolescence and the transition to early adulthood. Participants included 385 people between the ages of 17 and 19. They completed a series of questionnaires once a year for three years. The results of questionnaires on mobile phone use, anxiety, depression and self-regulation showed a moderate cross-sectional correlation. When these variables were examined longitudinally, in summary, problematic cell phone use was fairly stable during the transition from adolescence to early adulthood, and was associated with future depression (Coyne S. M., Stockdale L. & Summers K. [1]).

In one study, researchers used an experiment to investigate teenagers' mobile phone use. Researchers selected 439 students from a sample of Swiss students aged 12 to 17. A questionnaire was distributed first to their parents and then to the children (the process was repeated a year later with the same sample). The study concluded that nighttime cell phone use is common among young people. The report showed that people had a poorer perception of their health as a result of staying up all night. However, there was no recordable correlation between memory performance and phones. Reinecke has studied the mental health effects and stimuli of digital stress. He surveyed 1.557 German Internet users between the ages of 14 and 85 and reported that ac load was positively correlated with perceived stress and also had an indirect effect on depression and anxiety (Shoukat S. [12]).

There is not enough evidence on the potential risks to mental health from cell phone use. Therefore, researchers examined the relationship between mobile phone use and mental health by measuring levels of depression, anxiety and stress in Serbian and Italian university students. The cross-sectional study was conducted between March and May of the 2015/2016 academic year at two prestigious universities in Serbia and Italy and included 785 male and female students. Questionnaires on patterns and intensity of mobile phone use were prepared and developed by various published sources, as well as the Depression anxiety Stress Scale (DASS42), which is used to measure mental health. Statistical analysis showed that anxiety symptoms were more common among younger students, among those who wrote more text messages, and among those who used the Internet less often. Stress is more common in students who make fewer calls a day, as well in those who spend more time talking on the mobile phone per day. The strongest predictor of high stress levels was keeping the mobile phone less than 1 m away during sleeping. Conclusion: The intensity and mode of mobile phone use may be a factor affecting the causal path of college students' mental health problems (Višnjic Veličković, Sokolović Stanković, Mijatović, Stojanović Radulović [13]).

High cell phone use may cause anxiety, which is conducted by the article. The purpose of this study was to assess pathological Internet and mobile phone use among college students and to determine psychological, health, and behavioral correlations. A cross-sectional design was used to collect data from 337 students. The researchers developed two measures, the Internet Overuse Scale and the mobile phone overuse Scale. Other measures used were the Baker Anxiety Scale, the Baker Depression Scale and the General Health Questionnaire. Results: Internal consistent Logistic regression analysis of IOS and COS showed that excessive Internet use was associated with high anxiety; High cell phone usage was associated with women, high levels of anxiety and insomnia. The developed measure appears to be an effective tool for

assessing new behavioral addictions (Jenaro Flores, Gómez-Vela González-Gil Caballo [6]).

Social relations

This study explores that question in the framework of gratifications sought and their relationship both to differential cell phone use and to social connectedness. Based on a survey of Taiwanese college students, we found that the cell phone supplements the fixed telephone as a means of strengthening users' family bonds, expanding their psychological neighborhoods, and facilitating symbolic proximity to the people they call. Thus, the cell phone has evolved from a luxury for business people into an important facilitator of many users' social relationships. For the poorly connected socially, the cell phone offers a unique advantage: it confers instant membership in a community. Finally, gender was found to mediate how users exploit the cell phone to maintain social ties (Wei R. & Lo V. H. [7]).

Mobile phones play an important role in romantic relationships. They can be a source of uncertainty and conflict. While mobile phones can help partners in a relationship stay in touch, being able to reach each other all the time can lower the quality of their relationship. Setting and following rules about mobile phone use can help partners avoid relationship fallout from handling calls and texts in ways their partners may consider inappropriate or unacceptable. This study investigated the importance of mobile phones in romantic relationships and whether the presence of some mobile phone use rules predicted mobile phone use satisfaction and relationship satisfaction. The results show that mobile phones are important as a means of communication, and there is a strong positive correlation between satisfaction with mobile phone use and relationships. Rules about relationship problems and connecting with others help predict phone satisfaction. Rules about relationship issues, monitoring partner use, and repeated contact contribute to relationship satisfaction. Impacts, limitations, and future research are discussed (Miller-Ott A. E., Kelly L. & Duran R. L. [8]).

The co-evolution of social relationships and individual behavior in time and space has important implications, but is poorly understood because of the difficulty closely tracking the everyday life of a complete community. The researchers offer evidence that relationships and behavior co-evolve in a student dormitory, based on monthly surveys and location tracking through resident cellular phones over a period of nine months. Researchers demonstrate that a Markov jump process could capture the co-evolution in terms of the rates at which residents visit places and friends (Dong W., Lepri B. & Pentland A. [2]).

Anxiety is positively related with mobile phone addiction through analysing the study. Scientists investigated the relationship between psychological characteristics, mobile phone addiction and use of mobile phones for 269 Chinese female university students. They were all administered Rosenberg's self-esteem scale, Lai's personality inventory, and a mobile phone usage questionnaire and mobile phone addiction scale. The result shows that: 1) social extraversion and anxiety have positive effects on mobile phone addiction, and self-esteem has negative effects on mobile phone addiction; 2) Mobile phone addiction has a positive predictive effect on mobile phone usage behavior. The results of this study identify personal psychological characteristics of Chinese female university students which can significantly predict mobile phone addiction; female university students with mobile phone addiction will make more phone calls and send more text messages. These results are discussed and suggestions for future research for school and university students are provided (Hong F. Y., Chiu S. I., & Huang D. H. [4]).

Attention

Given that attention declines over time, scientists investigated when during lecture cell phones might impair learning. Across two experiments, participants watched a 20-min lecture under different cellphone conditions (keep or remove). Groups who kept their cellphones received distracting text messages during the lecture. There were quizzes for participants who

attended the lecture. Quiz questions were divided into four parts. Lastly, participants' nomophobia which means the fear of being without access to one's cell phone was assessed. Distracted participants performed worse on the test for the same material than those who were not distracted. Participants higher in nomophobia performed worse on the quiz for material that occurred in the 3rd quarter of the lecture. Findings indicate that having cellphones in a short lecture has its largest impact on attention and learning 10–15 min into the lecture. This study provides novel insights into the interactions between technology and learning to help educators and students optimize learning (Mendoza J. S., Pody B. C., Lee S., Kim M. & McDonough I. M. [9]).

Excessive cellphone use impacts attention and learning in classrooms. Ringtones are designed to draw attention away from on-going activities. In the present study, it was investigated whether the disruptive effects of a ringing cell phone on short-term memory are inevitable or become smaller as a function of exposure and whether (self-) relevance plays a role. Participants performed a serial recall task either in silence or while task-irrelevant ringtones were presented. Performance was worse when a ringing phone had to be ignored, but gradually recovered compared with the quiet control condition with repeated presentation of the distractor sound. Whether the participant's own ringtone was played or that of a yoked-control partner did not affect performance and habituation rate. The results offer insight into auditory distraction by highly attention-demanding distractors and recovery therefrom. Implications for work environments and other applied settings are discussed (Röer J. P., Bell R. & Buchner A. [10]).

Technology and environmental social factors have a relatively weak correlation with memory performance, which means it is insignificant. Another study examined the effects of exposing participants to a computer, friend, or neutral prime. Procedure order was also varied among the groups to determine whether potential memory failure would occur due to

an encoding failure or a retrieval failure. Participants were asked to write out a list of trivia statements either before or after learning while receiving either a computer, friend, or neutral prime. The data were analyzed with age, gender, year in college, ethnicity, high school GPA, college GPA, relationship status, hours online per day, and purpose of time online as covariates. No significant results were found. This information is still very important in determining how technology and environmental social factors impact memory performance and where future efforts should be placed in terms of strengthening and preserving our knowledge base (Han Xiu & Yu [20]).

The Current Study

The current study analyzes the research question of whether smartphone overuse has a negative impact on students' psychological well-being. Using a secondary data set, this study aims to test the following hypotheses:

Hypothesis 1: There will be a positive relationship between smartphone addiction and depression.

Hypothesis 2: There will be a positive relationship between smartphone addiction and anxiety.

Hypothesis 3: There will be a negative relationship between media use and sleep.

Methods

Participants

The present study has a sample size of 116 students with 42 males and 74 females. The age range of these participants were 18–25 years old.

Design

A correlation design was used to examine the relationship between smartphone use and psychological well-being, specifically we wanted to test the strength of the relationships between smartphone addiction and depression and anxiety, and the relationship between media use and sleep.

Procedures

In the original study, the participants of this study were recruited through a voluntary subject pool sign up. Students in this study received credit for participation.

Materials

Smartphone Addiction Scale- Short Version

The smartphone addiction scale is a 10-item questionnaire that measures each item on a 6 point scale. This scale is composed of questions that can tell the degree of addiction to smartphones. Through analysing each answer in the questionnaire, we can know the overall smartphone addiction level of an individual by calculating the total score.

Beck's Anxiety Inventory

The Beck's Anxiety Scale is a 21-question self-reported scale tool that measures and measures the severity of symptoms of anxiety. Participants responded to a series of statements in which they were asked a series of questions, such as "fearing the worst" and "having difficulty breathing." Each question was then rated on a four-point scale of 0–3, with higher scores indicating more severe anxiety symptoms. The entire scale calculates the total score by adding the scores for each of the 21 questions. Scores results are defined as follows: a score of 0–21 indicates low anxiety, a score of 22–35 indicates moderate anxiety, and a score of 36 and above indicates potential anxiety (Beck Epstein, Brown & Steer, 1988).

Beck's Depression Inventory

Beck's depression inventory II is a self-report tool that consists of 21 questions, and it helps to measure the degree of depression. Some sample questions that appear in this scale are "I feel I may be punished" and "I feel my future is hopeless and will only get worse", ect. Participants respond to a 4-point scale (0–3). The survey tooker those who got higher scores can be judged as a more severe situation. The scores in each item were then converted into descriptive scores: 0-13 was defined as minimal depression, 14-19 as mild, 20-28 as moderate, and 29-63 as severe. Total raw scores may range from 0 to 63. The BDI-II holds a Cronbach's alpha of 0.90, and this suggests adequate internal consistency (Beck Steer, & Brown, 1996).

Media and Technology Usage Scale

The media and technology usage scale is a 66 item questionnaire e on technology and media use,

and 18 items assessing attitudes towards technology. Eleven subscales were created for smartphone use, general social media use, Internet search, email, media sharing, texting, video games, online friendships, Facebook, phone calls, and TV watching. Four attitudinal subscales were created and defined: positive attitudes, negative attitudes, technological anxiety or dependence, and task-shifting attitudes. Sample questions asked about "how often do you do each of the following", including "how often do you watch TV shows, movies etc. on a TV set", "how often do you watch video clips on a TV set", "how often do you watch TV shows, movies etc. on a computer" and "how often do you watch video clips on a computer". (Rosen Whaling, Carrier Cheever, Rokkum [11]).

Results

The current study used a secondary dataset to analyze the relationship between smartphone addiction, depression, and anxiety. The secondary goal was to analyze the relationship between media use, sleep, and general media use. Researchers tested the following hypotheses:

Hypothesis 1: There will be a positive relationship between smartphone addiction and depression.

Hypothesis 2: There will be a positive relationship between smartphone addiction and anxiety.

Hypothesis 3: There will be a negative relationship between media use and sleep.

The results can be seen in (table 1 and table 2.)

Depression is positively related with smartphone addiction, and it is significant as the p-value is 0.005 which is smaller than 0.05.

Anxiety is positively related with smartphone addiction, and it is significant as the p-value is 0.004 which is smaller than 0.05.

Sleep is positively related with media use, and it is not significant as the p-value is 0.072 which is greater than 0.05.

Sleep is positively related with general media use, and it is not significant as the p-value is 0.199 which is greater than 0.05.

Table 1. – Pearson's Correlations

Variable		Smartphone Addictio	Depression	Anxiety
1. Smartphone Addiction	Pearson's r	–		
	p-value	–		
2. Depression	Pearson's r	0.259**	–	
	p-value	0.005	–	
3. Anxiety	Pearson's r	0.268**	0.670***	–
	p-value	0.004	<.001	–

* $p < .05$, ** $p < .01$, *** $p < .001$

Table 2. – Pearson's Correlations

Variable		Media Use	Sleep General	Social Media
1. Media Use	Pearson's r	–		
	p-value	–		
2. Sleep	Pearson's r	0.166	–	
	p-value	0.075	–	
3. General Social Media	Pearson's r	0.308***	0.120	–
	p-value	<.001	0.199	–

* $p < .05$, ** $p < .01$, *** $p < .001$

Discussion

For three distinct groups – smartphone addiction and depression, smartphone addiction and anxiety, and media use and sleep – we defined each variable with rigorous based on different scales, including *Smartphone Addiction Scale- Short Version*, *Beck's Anxiety Inventory*, *Beck's Depression Inventory*, and *Media and Technology Usage Scale*. Smartphone addiction refers to a behavioral condition of excessive use of mobile devices. It is usually defined and quantified by the number of times a user uses a mobile device or the total time spent online in a given period of time. Depression can be operationally defined as someone's score on a pen-and-paper depression scale, such as the *Beck's depression Scale* that we used in this experiment. According to the total score of the respondents and the performance of the questionnaire, the degree of their depression disorder was judged and acclaimed. Similarly, anxiety is another potential mental disorder. By using *Beck's Anxiety Inventory*, we defined the different degree of different symptoms of anxiety.

Looking at the big picture, the first hypothesis was that there would be a positive relationship between smartphone addiction and depression. Then we hypothesized that there would be a positive relationship between smartphone addiction and anxiety. The third hypothesis is that there would be a negative relationship between media use and sleep. The first hypothesis and the second hypothesis are both supported by the data. However, the third hypothesis is not supported by the data. Perhaps the first and second hypotheses were supported because nowadays smartphones are ubiquitous, and phones are in our lives as a necessity. People depend on smartphones, including its entertaining function, different apps, appealing websites, etc. Admittedly, people cannot live without it because it creates convenience. Nevertheless, if people stay away from their smartphone, they may feel frustrated and depressed. Moreover, they may have mental disorders such as depression and anxiety.

It also depends on the way that people use smartphones and the apps they use. Scientists should focus

on media use and sleep in the future studies because media use is related with smartphone addiction. Scientists may find a different relationship between media use and sleep.

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Guoer Zheng,

George School, Pennsylvania, USA

E-mail: camellia_zheng@outlook.com

NUDGES ON PEOPLE'S DECISION TO TAKE COVID-19 VACCINE

Abstract. This paper is targeted at the covid-19 pandemic and according to medical approaches. This research aims to examine the factors related to people's decision to take vaccines and develop a nudging strategy to enhance voluntary vaccine uptake. The linear regression model and behavioral economics principles help explain the relativeness between social, political, and economic factors and taking vaccines among people in America.

Keywords: Covid-19 pandemic, vaccination, behavioral economics, nudges.

1. Introduction

Since the FDA issued emergency use authorization for the first Covid-19 vaccine on December 11, 2020, the vaccine's effectiveness in managing the pandemic situation and reducing the infected cases had been a central argument.

Several determinants associated with the decision to take vaccines include the perceived safety and efficacy of the vaccine and the social, financial costs along with disease infection; (Streefland [25]) (François et al. [9]) individuals' vaccination decisions are also subjected to the impact of social influence. (Larson et al. [14]) For instance, suggestions from health professionals (Zijtregtop et al. [31]) and health-related newscasts would change people's perceptions of vaccine safety and efficacy (Brebán [3]). Factors such as religious belief, community opinion and literacy rate, health insurance coverage, employment situation, and even political party stand may play an essential role in people's decision to get vaccinated.

By using behavioral economics and psychological experimentation to develop theories about decision-making, people's perceptions, and preferences in the context of the covid-19 pandemic and the features that alter people's behavior can be better understood. Furthermore, since vaccination decision-making is not merely a process of payoff optimization but also an individual's response to

the impact of social influence, (Xia & Liu [29]) it is crucial to understand the incentives and concerns that drive or hinder people's decisions.

Similarly, complications like misinformation, vaccine hesitancy, and mistrust in the medical system have necessitated efforts to guide people in making the appropriate choices. Therefore, designing a new nudge that targets the covid-19 situation and fits the correlation trend between subjective factors and people's choices will result in prompter and rational response.

This paper overviews the general trend of vaccine uptake with the supporting theory of behavioral psychologic principles to weigh the factors that shape people's attitudes toward nudges and override people's previous concerns regarding vaccination, especially during the past several months. Recognition of factors associated with people's decision in taking vaccines during this early vaccination preparation period will help increase people's awareness of punctual healthcare, inform future strategies to welcome an increased rate of vaccination under emergence, as well as ensure equitable COVID-19 vaccine access indirectly, which will lead to an enormous change in the health rate in America.

2. Background

The zoonotic origin of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China. (World Health Orga-

nization, 2020) Community transmission of coronavirus disease 2019 (COVID-19) in the United States was first detected in February 2020. By mid-March, all 50 states, the District of Columbia, New York City, and four U.S. territories had reported cases of COVID-19 (CDC COVID-19 Response Team, 2020).

Despite the worsening economic situation and healthcare problems, state and national governments have adopted many approaches to curb the pandemic and address the wide-spreading problem. In the first months of the SARS-CoV-2 outbreak in the United States, states enacted restrictive SDMs intended to reduce transmission by limiting human-to-human contact (Miller et al. [19]). At the same time, the advice on masks and lockdowns as the policy remained conflictual.

In December 2020, two vaccines were granted an emergency use authorization (EUA) by the U.S. Food and Drug Administration (Johns Hopkins Coronavirus resource center [12]). The pandemic has triggered widespread misinformation that has undermined both understanding and acceptance of science and public policy, which has extended to vaccine acceptance (de Figueiredo et al. [7]). Although concerns and distrust in vaccine led some people to refuse such medical method, intent to receive COVID-19 vaccination increased among adults and across all priority groups, revealing that people choose to turn to vaccination as a means of problem solution and guardianship (Nguyen et al. [20]).

3. Literature Review

Geographic variation in numbers of Covid-19 cases and deaths likely reflects differences in epidemiologic and population factors as well as clinical and public health practices. (CDC Covid-19 Response Team, 2020) Meanwhile, differences in the availability and testing approaches and experiments likely have contributed to geographic differences in the vaccination uptake percentage.

From its principle, vaccination stands at the intersection between individual and society, which involves balancing an individual's decision to accept

or refuse a vaccine and the benefits to public health from community immunity when large numbers are vaccinated. For optimal success, vaccination programs need a high level of uptake. Because of such a vital requirement for consistent cooperation, the implementation of vaccines faces multiple challenges in popularization and promotion. Vaccine hesitancy, the delay in acceptance or refusal of vaccination despite the availability of vaccination services, (MacDonald & SAGE Working Group on Vaccine Hesitancy [18]) is therefore being used to describe such initial or periodic rejection towards the medical treatment.

In research in which two sequential large-scale randomized controlled trials (RCTs) are being used to investigate whether nudging people to get vaccinated via reminders carefully designed to reduce barriers to follow-through can improve Covid-19 vaccine uptake, results show that behavioral science insights can increase and speed up Covid-19 vaccinations at close to zero marginal cost. While promoting vaccinations at scale requires a multifaceted approach, findings suggest that behavioral nudges could be an impactful strategy to consider (Dai et al. [6]).

Existing studies on vaccination decision-making during pandemics typically focused on the analysis of hesitancy to receive vaccination (Khubchandani et al. [13]) and different barriers that prohibit such promotion, (Zhang & Fisk [30]) and the shifting of attitudes in taking vaccines before the publication of immunization (Pogue et al. [21]). However, with the updated data source for the vaccination rate and change in people's response regarding the pandemic, we can better generate a more accurate and up-to-day analysis in terms of people's decision in getting vaccinated in the Covid-19 pandemic case specifically by using behavioral economics and psychology as a backup explanation.

4. Influential Factors

Many possible underlying assumptions about the change in people's attitudes and opinions regarding vaccination have been associated with the under-

going situations. For example, people were having greater intent and feeling for improving their life quality and were their minds affected mainly by a media campaign and political regulations. In addition, education level and insurance coverage limit people's accessibility and economic capability and contribute to the variance in people's decision to take vaccines. By generating regression models for the collected data and analyzing behavioral and social studies, we narrow down the influential features to six different factors.

4.1 Reliance on Vaccination

One factor would be the increased awareness of the effectiveness of vaccination. For instance, the wide availability of vaccination has slowed down the increment of death rate and reported cases significantly starting from January 2021. In addition, the amelioration of the pandemic situation, which proves the necessity of vaccines, has led many people to be more determined about altering the problematic status of Covid-19, believing in the efficacy of masks and scientific guidance on controlling the pandemic, and most importantly, having more vital willingness to take a Covid-19 vaccine when available.

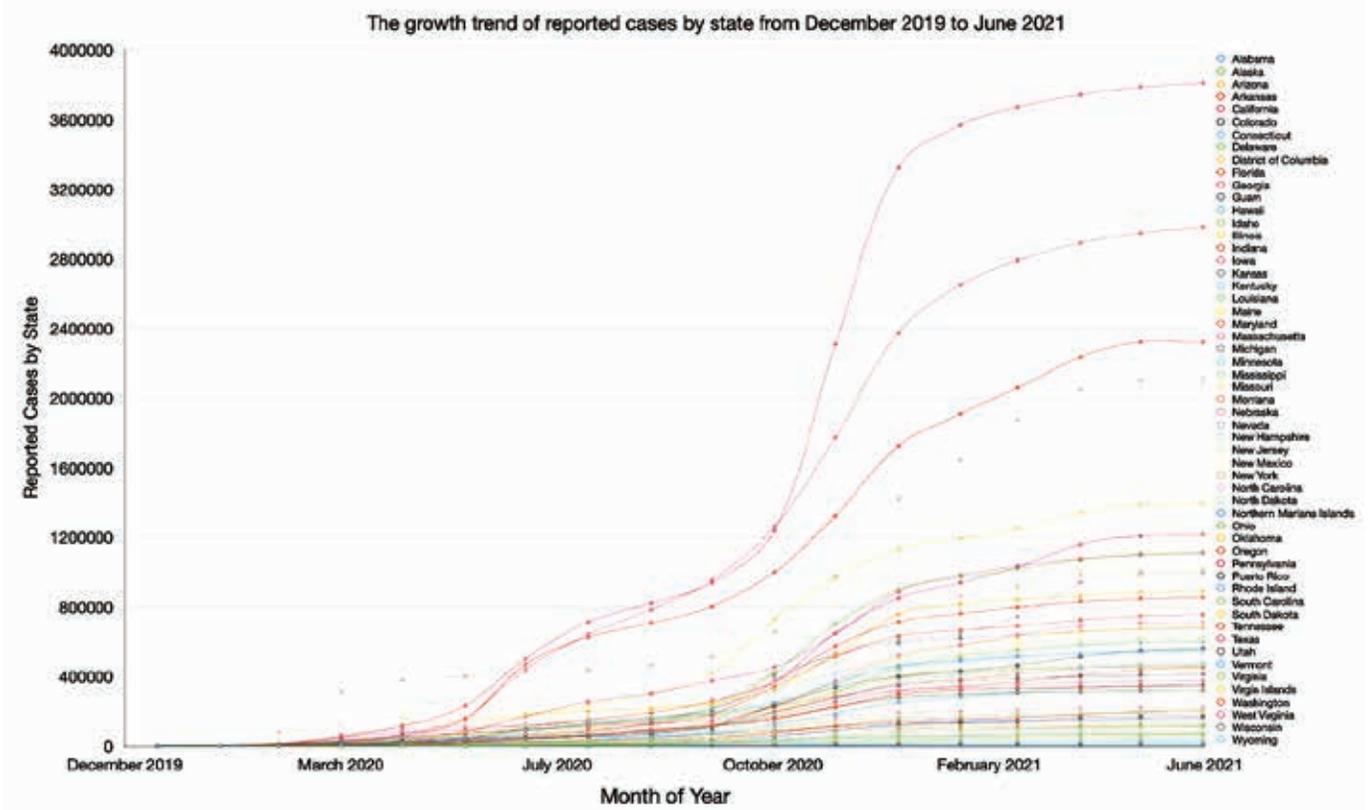


Figure 1.

The desire to get back to work and recover from the economic loss also led both the officials and individuals to pay closer attention to the availability of vaccination. Especially for ethnicity and low-income families who face tremendous challenges living and covering the medical expenses, they need to secure the stability of their occupation oppor-

tunity. With such strong intent to live an everyday life after a whole year of lockdown and emergence, many chose to take a dose shot to reduce the probability of infection and assure themselves of their safe travel plan. Furthermore, the duration of time surpasses people's previous concern about the safety and feasibility of vaccination in a dilemma.

People in doubt, especially those who worry that vaccines have been adopted too quickly without enough safeguard tests and may result in unpredict-

able side effects, are reassured as they view mostly successful cases and the considerably delightful trend from the data source.

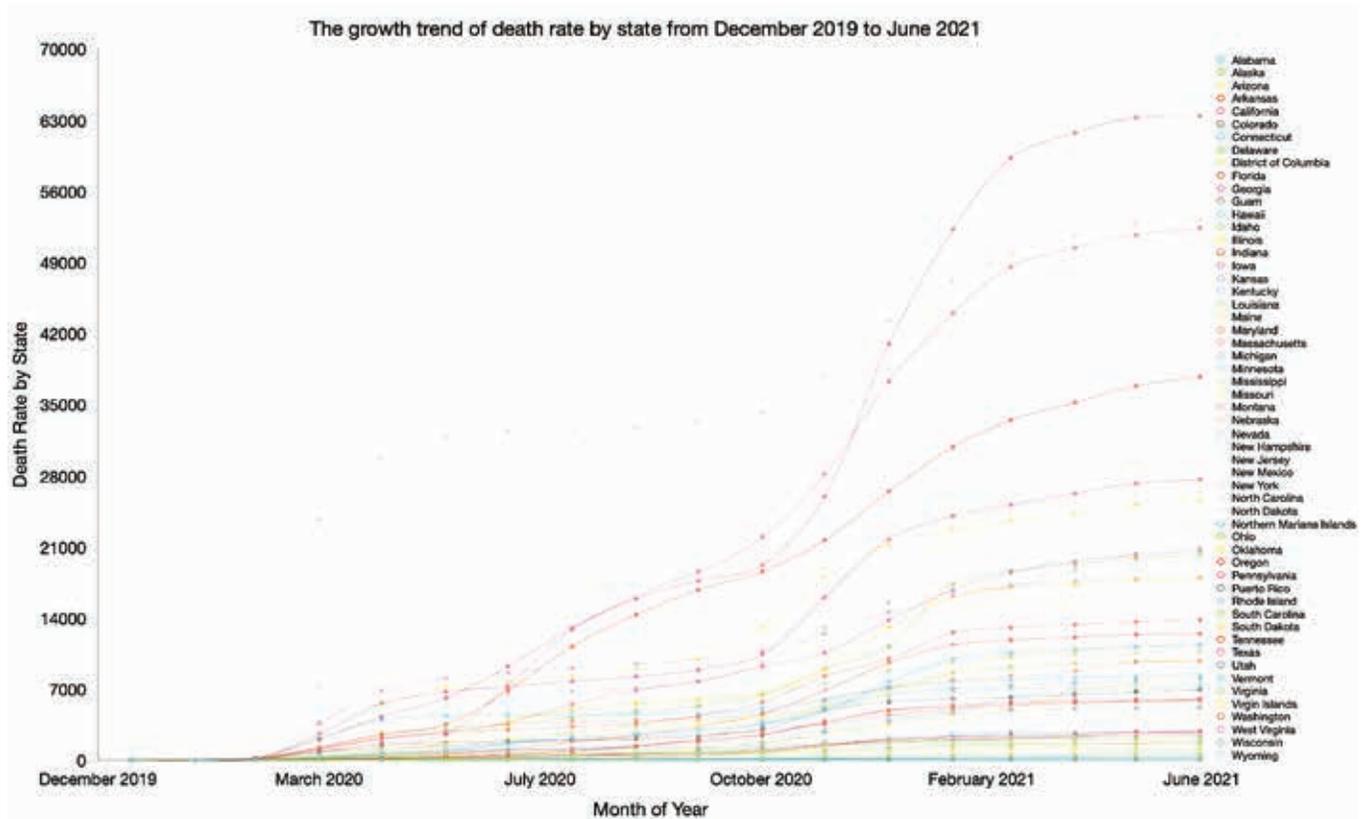


Figure 2.

Data source: Covid-19 data, US-States-History, CSV, June 2021

4.2 Literacy Rate

Collective literacy skill levels and access to professional knowledge affect the implementation of vaccination programs. A significant influence of education – including university degrees – on vaccine acceptance has been observed in many studies. Health literacy, the degree to which individuals can obtain, process, and understand basic health information and services needed to make appropriate health decisions (Biasio [2]), is also part of the influential incidences.

Since familiarity with medical knowledge predominantly affects people's decision to approach scheduled medical meetings and receive vaccines on time, literacy rate, primarily medically targeted acknowledgement is closely related to the acceptance of the vaccine. From the linear regression generated by the online data, a direct relationship can be observed between literacy percentage and percent of the total population fully vaccinated by the state of residence.

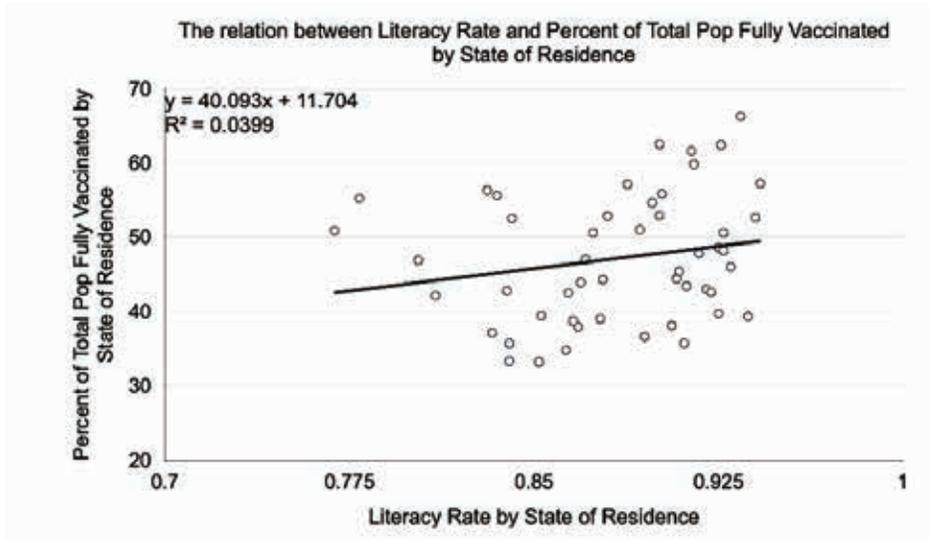


Figure 3.

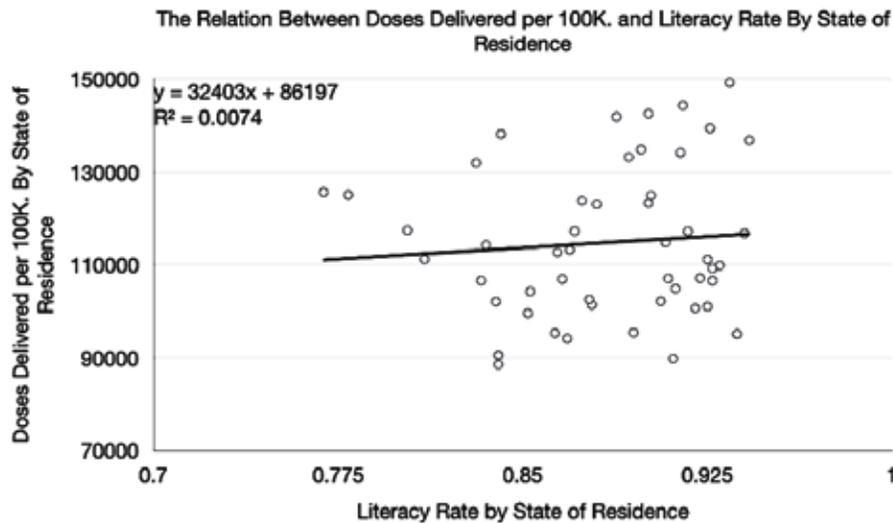


Figure 4.

Data source: *The Condition of Education 2020, US. Department of Education, May 2020*

4.3 Medicare and Health Insurance

In addition to literacy rate, people’s awareness of medication is another determinant for vaccination. The cost has always been a barrier to receiving and providing timely preventive medical care to children living in poverty (Smith et al. [23]).

According to a study that examined the impact of health insurance status on vaccination coverage among adult populations, adults without health insurance were significantly less likely than those with health insurance to be vaccinated for influenza, pneu-

mococcal, and Tdap after adjusting for confounders (Lu et al. [17]).

A similar trend is also shown as a result of the Covid-19 vaccination case. Based on the linear regression graph on the data source from Health Insurance Coverage in the United States: 2019 by US Department of Commerce, United States Census Bureau, the percent of the total population fully vaccinated by the state of residence is highly associated with the percent of the total population with health insurance coverage in 2019.

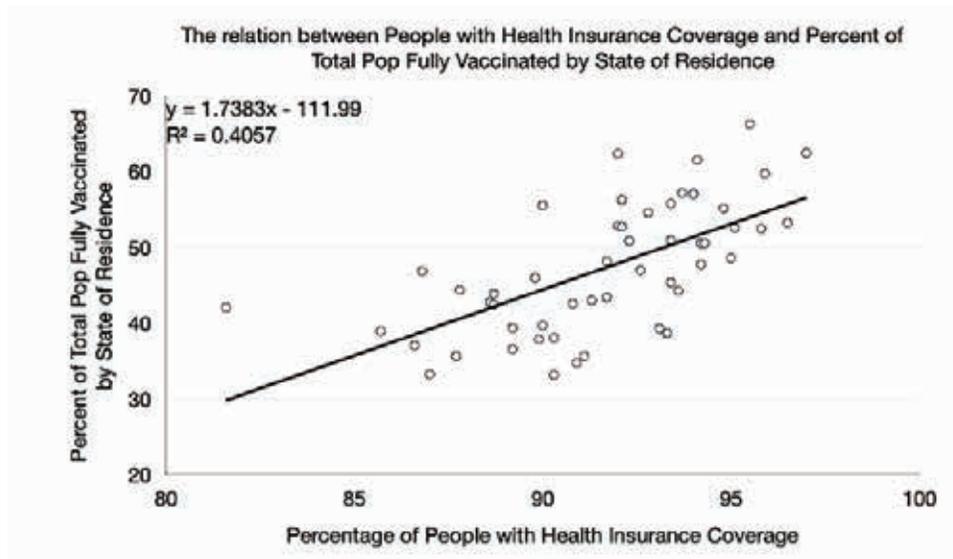


Figure 5.

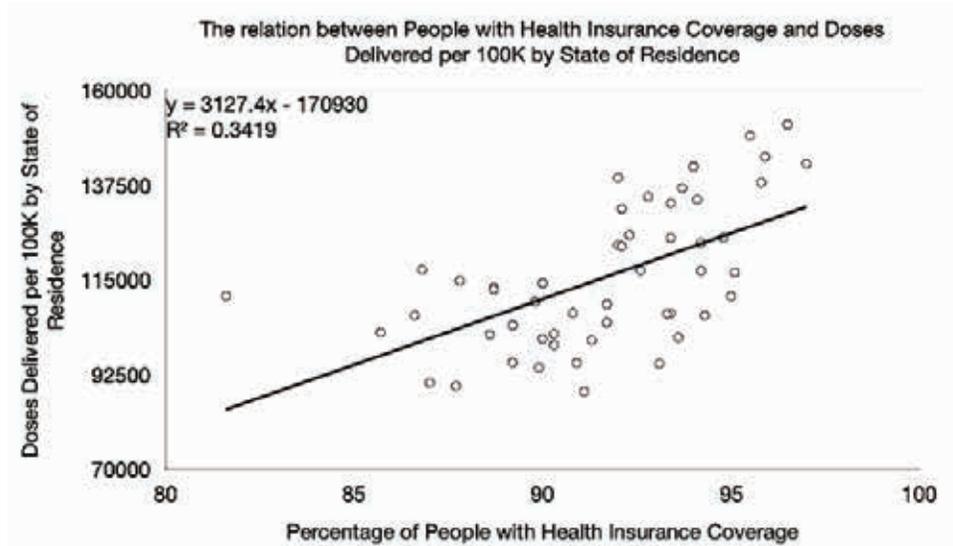


Figure 6.

Data source: Health Insurance Coverage in the United States: 2019, Department of Commerce, U.S. Census Bureau, September 2020

4.4 Partisanship in Engagement

The pandemic response has also become increasingly politicized. Generally, republican governors were less likely to enact policies aligned with public health social distancing recommendations at the beginning of the pandemic (Adolph et al. [1]).

Such a trend extends to the point of vaccination acceptance that states that voted Republican in the last election and have republican governors tend to have a lower vaccination rate. The average percentage

of the total population of fully vaccinated by the state of residence for states that voted for the Republican party in last election is about 41.6. The states that voted for the Democratic party in the last election is about 53.1; the average of the percentage of the total population fully vaccinated by the state of residence for states under the governance of the Republicans is 43.6, while that for states under the governance of Democrats is 51.3.

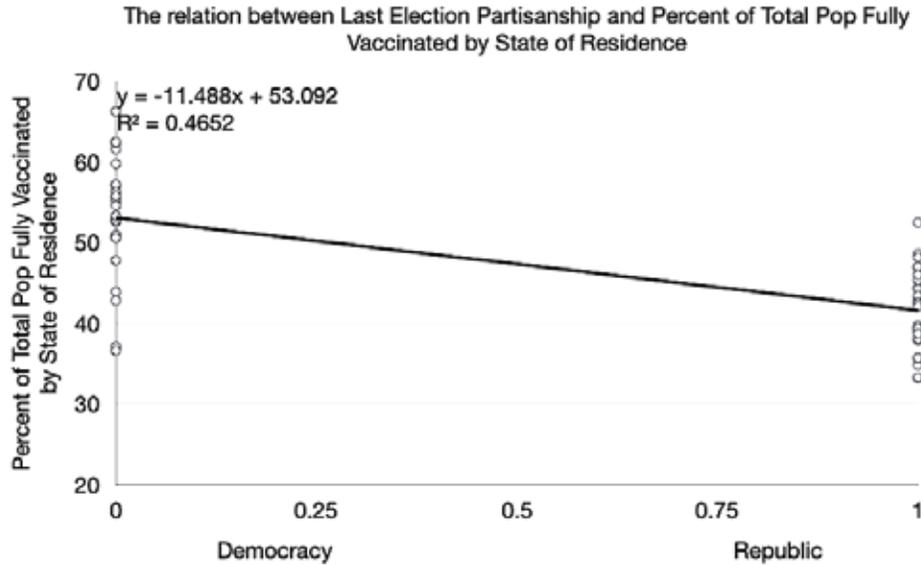


Figure 7.

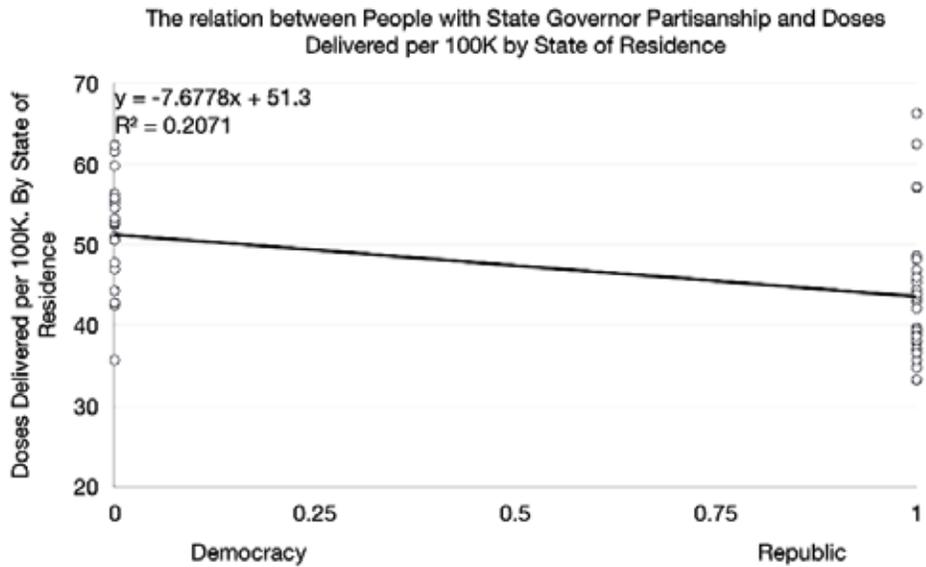


Figure 6.

Data source: 2020 Election Result and 2021 state governor partisanship, National Archives

4.5 Mass Media Campaign and Coverage

The nature of new media platforms poses challenges for thinking about the effects of and remedies against misinformation in the very openness of Internet-based platforms to all sorts of content producers, resulting in the accuracy of delivering message becomes a matter of issue. Since some misinformation that receives widespread attention does not warrant intervention by public health institutions, the impact of such audience exposure vastly outweighs

what relatively limited public health media campaigns are capable of a hindrance (Southwell et al. [24]). Especially when the comprehensive reporting on vaccination is unavailable, the most common choice becomes the option that most assures people relying on the simplest way of attaining information and making choices.

Due to the scale of the targeted audience, a message reaches, the consequence of such influence can sometimes be massive. For example, when Trump

reversed a plan for White House officials to receive vaccine in mid-December, his proponents and followers may swiftly change their minds about the vaccination plan. On the contrary, the popular trend of posting the “I Got Vaccinated” sticker on Instagram and Facebook in May can work the other way around. The sticker serves as a gentle social pressure, reminding people who may have forgotten to do it and calling for joint efforts. Leading by many popularities and stars with tens and hundreds of millions of followers, mass media drives more people to take the vaccine in a short period as celebrity endorsement can cut through the concerns and make people consider options they may have outright rejected using an encouraging and persuasive message.

Even though media platforms can be misleading, advertising campaigns can necessarily prevent and respond to the inaccurate information promptly and professionally, and more importantly, introduce people to updated medical adoptions and plans.

4.6 Endorsement and Regulations

Trust in the vaccines is also critically dependent on the ability of governments to communicate the benefits of vaccination and deliver the vaccines safely and effectively, which makes government actions of significant importance in terms of combating the declining compliance with public health-related rules. In addition to scientific validation, policymakers have developed and endorsed policies and environmental support systems that foster the promotion of Covid-19 vaccination programs (Khubchandani et al. [13]). These organizations’ endorsements successfully increase individuals’ willingness to receive a vaccine.

While endorsements turn out to be motivating people’s decisions many people also change their minds due to the regulations set by the government. Starting from June, employers could legally require Covid-19 vaccination for employees to re-enter the workplace and provide incentives to encourage employees to get a shot. Similarly, New York City would require proof of vaccination to enter all restaurants, fitness centers, and indoor entertainment venues in

early August. Applying a limit on access to the workplace and public facilities pushes people who regard vaccination as low importance even further to their vaccination action. Either running out of choice or intentionally reconciling with previous worries, the motive to devote all attention to the right to share the public resource equally becomes one of the primary reasons to take the vaccine.

5. Behavioral Economics and Psychological Mechanics Principles

5.1 Nudging

Nudges, any aspect of the choice architecture that alters people’s behavior predictably without forbidding any options or significantly changing their economic incentives (Sunstein [12]), pushes people in the direction that is perceivably “right” and “logical” by encouraging people to make better decisions (Halpern et al. [10]). While one mode of thinking called reflective thinking enables us to make rational decisions by considering all the pros and cons of each choice, the other named automatic thinking allows us to make quick decisions with little effort.

5.2 Defaults

Some of the most consistent and significant nudge effects arise out of the manipulation of defaults. Default is the course of events that will transpire when a person does not actively choose an alternative path. Though the quality of evidence varies across domains and contexts, defaults have been shown to affect several decisions, many of them related to health, such as getting vaccinated against influenza, donating organs for transplantation, and selecting specific options within advance directives (Choi et al. 2002).

5.3 Mental accounting

Mental accounting is defined as a type of decision framing in which individuals form psychological accounts containing the advantages and disadvantages of an event or option. (Henderson & Peterson [11]). This concept has been used to explain violations of the principle of fungibility in examinations of saving behavior (Shefindz Thaler [15]) as well as decisions involving monetary gains and losses, as the starting

point for a model of consumer behavior (Thaler, [15]).

5.4 Prospect theory

Prospect theory assumes that losses and gains are valued differently, and thus individuals make decisions based on perceived gains instead of perceived failures. Losses cause a more significant emotional impact on an individual than makes an equivalent amount of growth. Given choices presented two ways – with both offering the same result – an individual will pick the option offering perceived gains (Tversky & Kahneman [27]).

6. Application of Principles on Factors Explanation

When making decisions, people usually do not weigh outcomes by their objective probabilities but rather by transformed possibilities or decision weight based on their subjective preference and evaluation. Moving from the editing phase that involves interpreting options of different vaccine types and making judgments of their applicability, to the evaluation phase where people make a final decision about whether to take the vaccination, their way of processing information leads to different outcomes choosing from the same choices, and this is when the isolation effect occurs.

The nature of the decision-making process being interest-driven rationalizes the change in people's response to vaccine uptake. Either under the influence of political partisanship or because of a high degree of education background, people with (or people who perceive to) have a higher possibility of infection are more likely to get vaccinated, which can be explained by the certainty effect of the prospect theory. The certainty effect is exhibited when people prefer specific outcomes and underweight outcomes that are only probable, leading individuals to avoid risk when there is a prospect of a sure gain and contributes to those seeking risk when one of their options is an inevitable loss (Tversky & Kahneman [27]). When health risk is involved in the decision of vaccination and the probability of different unprecedented

symptoms is unknown, those who understand infection as a sure loss would choose to take the risk and get vaccinated as preventive measures, while those who do not perceive the pandemic as a significant threat but rather fear the possible side effect of vaccine would avoid the attempt of taking the vaccine.

Further, peer influence on media platforms or in-person is related to a psychological mechanism, heuristics. These mental shortcuts are used in situations in which people assess the frequency of an event belonging to a class or its probability (Tversky & Kahneman [27]). When unsure how to act in a given situation, we solve problems by substituting unavailable information with a cue in the environment or by looking at and imitating others' actions. The popular trend followed by the pressure of involvement and norms temptingly makes people more susceptible to cognitive biases, systematic deviations from rational judgment.

Significant detriments as health insurance coverage and government regulations are correlated with status quo bias, which tends to place higher values on options perceived as status quo, explained because of loss aversion (Tversky & Kahneman [27]). Since financial crisis on the national level also has an unneglectable impact on individuals, families already under tremendous economic pressure tend to avoid any additional or unnecessary expenses but focus more on balancing every bill in an organized and planned-out manner. On the other hand, people capable of categorizing vaccination and the risk of infection to the "status quo" region would place vaccination as the most urgent task before all. Cognitively biased preference over health and safety at hand makes people want to get vaccines regardless of the cost or other sacrifice needed. Governments enforced policies such as regulations on entry to restaurants and other public spaces. Perception of these limitations concerns citizens as they feel a loss of freedom. As a result, overall wellbeing declines.

7. Design of Nudges

Behavioral economists have identified striking ways in which trivial differences in the presentation of

options can powerfully and predictably affect people's choices. To maximize vaccinations in a population, it is critical to understand how to best design behavioral interventions to either boost intentions to get vaccinated, remove barriers to follow-through on good intentions, or do both (Brewer et al. [4]). By developing a system that helps people make more efficient and rational decisions and achieves states of affairs that are more socially desirable in the eyes of nudging candidates, the problem of extreme vaccination hesitancy and misconception can be addressed more appropriately (Lepenies & Małecka [16]).

Scientific organizations, public health experts, media outlets, and clinic advertising have been educating the general population about the Covid-19 vaccine. Meanwhile, the shared incredible or false information about lockdowns, vaccinations, and death statistics, have fueled the panic of purchasing products and exacerbated insecurity with a state of fear and panic among the public (Elhadad et al. [8]).

The spread and circulation of misleading information about the vaccination and its impact are ubiquitous, which reduce people's confidence in the government and medical centers. Therefore, managing the spread of misleading and incredible information can perform well as a nudge that changes people's minds about vaccination.

In the public sector, governments and public hospitals play an essential role in assuring the published data source's validity and promptly detecting unreliable reports. 1) Reviewing the collected ground-truth data with scientific experiments as a backup before releasing speech and reports; 2) establishing a particular department or collaborating with third-party service in charge of identifying misleading information; 3) teaching the public, especially employees and students, the fact about vaccination and its applicability by creating promotion pamphlet; 4) adjusting and introducing new insurance and welfare policies corresponding to the pandemic situation by taking more economic aid into consideration.

In addition to the official governments and medical centers, large corporations and social network platforms matter. Hiding behind the screen and keyboard, many take advantage of the distance and lack regulation to eliminate the responsibility they are accounted for when publishing hoaxes and posting false news. With a single click, inauthentic reports would reach hundreds of accounts in one second, which is unpredictably powerful and dangerous. Thus, the following procedures are worthy considering: 1) Disrupting invalid advertising method such as economic incentives and misleading titles in advertisements and inflammatory articles for traffickers of misinformation; 2) Applying machine learning on the fact-checking system to assist in detecting fraud and lead the public to better control misleading news from the source; 3) Limiting the access to buying ads or trending flows through stricter enforcement of policies to reduce the chance of quick spread at scale; 4) making it easier to report a false news story on platforms such as Facebook and Instagram, for instance, by simply clicking a button so that stories that are flagged as false might show up at a lower frequency.

8. Conclusion

This research examines the influential factors regarding the variance in vaccination uptake trend among states in America. The regression line model and mechanism analysis yield that reliance on vaccination, literacy rate, Medicare and health insurance, partisanship in engagement, mass media campaign coverage, and endorsement and regulations have an essential impact on people's decision to take the vaccine. By using behavioral economics principles such as nudging, defaults, mental accounting, prospect theory and other terms, not only were the underlying correlation between nudging factors and the resulting behavior being exposed, but also were some nudges targeted at eliminating misinformation being successfully designed to address the problem of vaccination hesitancy and boost vaccine uptake intentions among people.

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Section 4. Sociology

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Selina Zheng,
The Bishop Strachan School in Toronto, Canada
E-mail: selinazhenghanyi@gmail.com

THE ASSOCIATION BETWEEN SMARTPHONE USE AND PSYCHOLOGICAL WELL-BEING AMONG COLLEGE STUDENTS

Abstract. People's overdependence on smartphones have led them into an abundance of psychological well-being issues. Various literature has examined the association between digital-screen engagement, addictive behaviours, and mental well-being. To develop a deeper understanding in the correlation among these factors, the current study aims to find the relationship between smartphone use and psychological well-being, specifically on how students' media use has led them to mental health issues such as addiction, depression, anxiety, sleep problem, and the fear of missing out (FoMO). The results supported hypotheses 1, 2, and 3, smartphone addiction correlates with anxiety, depression, and FoMO; however, the results of the study do not support hypothesis 4, in which there is no correlation between smartphone addiction and sleep issues. In conclusion, smartphone overuse and addiction may subsequently affect an adolescent's mental well-being.

Keywords: smart phones, FOMO (fear of missing out), depression, anxiety, social science experiment.

Introduction

Smartphone Addiction

People's reliance on technology, mainly smartphones, have led to serious psychological health issues. Experimental literature may help researchers with a deeper understanding of the impacts of smartphone overuse. A study examined the relations between smartphone engagement and psychological well-being using time-use diaries and retrospective self-report data obtained from three countries: Ireland, the United States, and the United Kingdom (Orben Przybylski [15]). The authors stated that current screen-time measurements lack quality as self-reports appear to have inaccurate answers: participants overestimate or underestimate their daily

use of phones. It is believed that young people's difficulties in relaxing after engaging in stimulating technology use are indirectly associated with lower psychological well-being and delayed bedtime. The study aims to explore whether engagement in smartphones has reliable, measurable, and substantial associations with the psychological well-being of young people. The study then found little evidence for substantial negative associations between digital-screen engagement and adolescent well-being (Orben Przybylski [15]).

In fact, an increasing number of reports and articles have talked about how people's overuse of smartphones has interfered with their daily lives and mental well-being. A correlation between smartphone use

and psychological well-being was examined among university students with control over important variables they think previous studies didn't have. This was a cross-sectional study conducted from January to March in 2018 among university students in Thailand using the Flourishing Scale and the eight-item Young Diagnostic Questionnaire for Internet Addiction. The researchers defined students whose scores are above the median value as excessive smartphone users. The results showed that students with excessive use of smartphones had lower scores in psychological well-being than those who did not use smartphones excessively. (Tangmunkongvorakul Musumari, Thongpibul Srithanaviboonchai, Techasrivichien Suguimoto, Ono-Kihara & Kihara [19]).

The influence of smartphone overuse could be studied through alternative ways—understanding the impact of excessive and nocturnal use of social media and technological devices on users' well-being also provides us with insight into how young adults' behaviours are influenced. A report on young adults in the U.K. estimated that about 20% of respondents frequently awoke at night to check social media notifications which caused them to experience more exhaustion than their peers. Researchers believed that the maladaptive use of smartphones and compulsive social media might affect young people, especially young people's work efficiency and sleep hygiene; therefore, specific habits or behaviour could be changed significantly. The study aimed to contribute to the existing knowledge on the potential effects of FoMO (fear of missing out) and CSMU (compulsive social media use) on individuals' sleep behaviour (Tandon Kaur Dhir & Mäntymäki [18]).

Another study that showed an analysis between various factors was from Billieux (2012), who proposed to describe problematic mobile phone use through four paths: an impulsive path, a relationship maintenance pathway, an extraversion pathway, and a cyber-addiction pathway. The study aimed to understand better how problematic mobile phone use is related to health-related quality of life (HRQOL),

including mental health and behavioural problems in adolescents while controlling for the amount of mobile phone use. After the surveys they created and a series of data they analyzed, they concluded that problematic phone usage is associated with external factors such as worse home and school environments and internal factors such as impaired HRQOL and behavioural problems (Roser Schoeni Foerster & Rössli [16]).

Anxiety, Depression, and Addiction Caused by Cell Phones

To dive into a more specific consequence of phone addiction, mental health problems such as Anxiety and Depression are considered significant to look at. One study's objective was to identify the relationship between smartphone addiction with anxiety and depression among undergraduate students in one of the local universities in Malaysia in September 2016. The authors distributed a self-administered questionnaire including five sections on the participant's cell phone usage details. This study highlighted the relationship between smartphone addiction with anxiety and depression. Students who reported high scores of smartphone addiction tended to report high scores of anxiety and depression (Ithnain Ghazali & Jaafar [7]).

It is confirmed that cell phone use may have a great impact on mental well-being. Some researchers examined the relationship between mobile game addiction and social anxiety, depression, and loneliness among adolescents. They found that mobile game addiction was positively associated with social anxiety, depression, and loneliness. The study also found a gender-based difference in mobile game addiction. Male adolescents tend to report more social anxiety when they use smartphones addictively. However, this study focused more on gender-based differences in cell phone use; they discovered that compared with female adolescents, male adolescents tended to lack social skills, were more socially withdrawn and disclosed less about themselves in offline communication settings (Wang Sheng & Wang [20]).

Other researchers believe that gaining a thorough understanding of the complex relationship between well-being symptoms and screen time use will lead to more effective intervention strategies for improving teenagers' emotional and physical health. An article from 2019 synthesized the associations between screen-based sedentary behaviours, depressive symptoms, and anxiety symptoms among youth based on previous studies. The researchers systematically integrated the results from previous studies and summarized the moderators that potentially influence people's mental well-being. The results showed that when it comes to a technology-based moderate variable, computers and smartphone use affect people's well-being more than other technology such as TV because computers and smartphone use often involve social media and interactions, which are thought as essential variables that impact emotions. (Nuzzo Meyer Snyder, Rav, Lapascu, Souleles Andrada & Bishai [12]).

An abundance of studies all showed their observation of smartphone use and mental well-being's correlation; however, this literature started off from a slightly different perspective. It aimed to investigate the prevalence of smartphone addiction and its association with depression, anxiety, and attention-deficit hyperactivity disorder (ADHD) symptoms in a large sample of Korean adolescents (Kim Park, Kim Pan Lee & McIntyre [8]). The authors handed out surveys that require participants to report their severity in psychological well-being (symptoms, feelings, etc.) The study found that the total Korean Smartphone Addiction Scale score is positively correlated to the total Conners-Wells' Adolescent Self-Report Scale score, Beck Depression Inventory score, Beck Anxiety Inventory score, gender, smoking and alcohol use. Thus, the finding indicates that ADHD, depression, and anxiety may be significant risk factors for developing cell phone addiction. We found it interesting because, once again, well-being and phone use have fallen into the loop of constantly cycling and affecting each other. Similar to this study,

psychological health has inversely influenced phone addiction, whereas phone addiction affects psychological health in other studies (Kim et al. [8]).

Behaviors Affected by Cell Phone Overuse

Smartphone use could subsequently affect people's behaviours. One study focused on the effects of cell phone overuse on children's behaviours. As time passes, more children are starting to use cell phones at earlier ages. The authors examined the parental and postnatal influences on their children. Researchers found that these factors are associated with behavioural difficulties. The authors discovered that children are more easily impacted by various confounding variables during earlier ages, such as parental styles, environmental influences, social norms, etc. The article focuses more on the external effects children had during growth, especially the behaviours of mothers. For instance, children whose mothers have more exposure to stress would be negatively influenced and, therefore, increase cell phone use (Divan Kheifets Obel & Olsen [6]).

Addiction behaviours should be considered serious as well. (Billieux et al. [4]) stated that the dysfunctional use of cell phones involves "behavioural addiction" that shares similar symptoms as drug addiction. Their study compares and analyzes approaches—mainly a system-based approach and a process-based approach—and concludes that the addiction model can simplify an individual's psychological functioning. In other words, the authors believe that cell phone overuse is directly associated with behavioural addictions. People are rather normalizing cell phone overuse, and yet, the excessive use of these technologies would cause severe psychological problems. Addictions and FoMO could be great examples to represent the current status of people's phone usage. The approaches that the articles analyzed all stated that cell phone overuse is, without exception, problematic (Billieux Philippot, Maurage De Mol & Van-der Linden [4]).

Smartphone use may involve group interactions that could lead people to severe mental issues; the

harms are not limited to only addiction-caused issues. A study discussed addictions to cell phones and the potential risks people may experience while using phones. Cyberbullying is another significant factor of depression, anxiety, and other mental well-being issues. Unwanted exposure to photographs, videos, and personal info of the victim will cause panic, leaving shadows on people. The article started from this point of view, which is slightly different and novel than other articles, as this involves societal and group influences. Psychosocial issues caused by cell phone dependence may momentarily increase personal stress. Overall, the study shows that the riskiest causes of cell phone overuse and analyzes them by using previous studies and research (Sansone & Sansone [17]).

Effects of Cell Phone Usage on Social Behaviors and Interactions

Understanding the reverberations of smartphone overuse does not only assist us with avoiding its potential harm but also addresses concerns relating to social interactions. Researchers aimed to develop a theoretical model for which social effects of cell phone usage in public places documented in observational studies can be empirically tested. In one study, the authors discussed several variables considering cell phone usage and social interaction with proximate others. They also experimented with cell phone usage on the concept of social participation, mainly focused on helping behaviours. At the end of the experiment, they concluded that people who are on their phones while the accident happens are less likely to help. The authors believe that cell phone usage could distract people from social responsibilities, which means cell phones disturb people from interacting and getting along with more people (Banjo Hu Sundar [1]).

Another similar study focused on 193 student nurses selected through a stratified random sampling technique from a selected College of Nursing, Dehradun, Uttarakhand. The study aims to assess the impact of mobile phone usage on the psychosocial well-being of students. They compared four

variables to define the dependent variables: attention and concentration, academic performance, socialization and communication, and levels of phone addiction. The authors found that age and gender seem to be associated with levels of addiction, concentration, and attention. Female users seem to have a higher addiction to phones as they often use cell phones to communicate and socialize. The results showed that cell phones have a significant impact on students' concentration levels (Maurya Penuli Kunwar, Laila Negi Williams & Thakur [11]).

Involving theories from thinkers may lead us to another standpoint. A book written by Morrill [10] involves Erik Erikson's developmental psychology theory. The author believes that cell phone overuse has a significant impact on both children's and adult's development. One thing that was innovative to us is that the author examined relations between cell phone possession, cell phone use, and psychosocial and identity development using Erikson's Psychosocial Theory and Marcia's Adolescent Identity Paradigm. The author conducted an experiment in which a sample of 705 college students, ages 18–24, completed a questionnaire that measured the amount and type of cell phone use, identity development, psychosocial maturity, friendship attitudes, and school achievement. The data showed that cell phones have now infiltrated our lives (Morrill [10]).

The current study analyzes the research question of whether smartphone overuse has a negative impact on students' psychological well-being. Using a secondary data set, this study aims to test the following hypotheses:

Hypothesis 1: There is a positive relationship between cell phone addiction and Anxiety.

Hypothesis 2: There is a positive relationship between cell phone addiction and Depression.

Hypothesis 3: There is a positive relationship between cell phone addiction and the fear of missing out (FoMO).

Hypothesis 4: there is a positive relationship between cell phone addiction and sleep issues.

Methods

Procedure:

In the original study, each participant was recruited via the psychology subject pool and from the general student population at UA. Students enrolled in PY101 will receive 2.5 credits towards the research requirement for the course when they participate in the study. Deception and concealment of the study's main purposes are necessary to eliminate participant bias for the memory task so researchers will state that the study is regarding the relationship between the campus atmosphere and students' psychological well-being. A consent form was signed by each participant and their personal information will be used solely for the purposes of providing them with credit for completion of the study, but the phone number was also used for texting the participants during the study as stated in the consent form.

During the experiment, participants were asked to complete a series of tasks and questionnaires that were designed to fulfill the experiment's aim, including a navigation task, a memory task, and a series of questionnaires regarding smartphone use and other measures discussed in the materials section.

The current study aims to understand the underlying mechanisms such as smartphone addiction, anxiety, or depression that may explain why chronic and short-term use of smartphones may influence spatial memory. Based on the specific psychological issues the study focused on, we are going to examine further the relation between smartphone usage and mental health.

Participants:

The present study has a sample size of 116 students with 42 males and 74 females. These participants were recruited from students enrolled in Psychology 101 course at a University in the South East and received course credit for participating in the study.

Design:

A correlation design was used to examine the relationship between smartphone use and psychologi-

cal well-being, specifically on how students' media use has led them to mental health issues such as addiction, depression, anxiety, sleep problem, and the fear of missing out (FoMO).

Materials:

Smartphone Addiction Scale, Short Version (SAS-SV)

The SAS-V is a 6-point Likert scale (1 "strongly disagree" to 6 "strongly agree"). This questionnaire holds internal consistency for each question and scale of the 10 items. In terms of concurrent validity, The SAS-SV was significantly correlated with the Smartphone Addiction Scale (SAS), Smartphone Addiction Proneness Scale (SAPS) and The Korean self-reporting internet addiction scale short-form scale (KS-scale). The SAS-SV also includes cut-off values that were determined based on the consultation results with the clinical psychologists. The cut-off values for each gender are different. In boys, the cut-off value was 31, the sensitivity value was 0.867, and the specificity value was 0.893. As for the girls, the cut-off value was 33, the sensitivity value was 0.875, and the specificity value was 0.886. Based on the cut-off values, this scale was considered as an appropriate tool for evaluating smartphone addiction. The SAS-SV uses total score ranges from 10 to 60, with the highest score being the maximum presence of "Smartphone addiction" in the past year. Overall, the SAS-SV holds content, concurrent validity, and internal consistency (Kwon Kim Cho & Yang [9]).

Beck's Anxiety Inventory (BAI)

Beck's Anxiety Inventory (BAI) is a 21-item self-report inventory for measuring the severity of anxiety. Individuals respond to a series of statements and rate how bothered they are by each item using a four-point scale (0-3), with higher scores indicating more symptoms of anxiety. BAI showed high internal consistency ($\alpha = .92$) and test-retest reliability over 1 week, $r(81) = .75$. The total scores are calculated by finding the sum of the 21 items. A score of 0-21=low anxiety, a score of 22-35 = moderate anxiety,

ety, and a score of 36 and above indicate potentially concerning levels of anxiety (Beck, Epstein, Brown, & Steer [2]).

Beck's Depression Inventory-II (BDI-II)

The Beck Depression Inventory Second Edition (BDI-II) is a 21-item self-report instrument intended to assess the existence and severity of symptoms of depression. When presented with the BDI-II, a patient is asked to consider each statement as it relates to the way they have felt for the past two weeks. Each of the 21 items corresponding to a symptom of depression is summed to give a single score for the BDI-II. There is a four-point scale for each item ranging from 0 to 3, with higher scores indicating more severe symptoms of depression. BDI-II showed high internal consistency ($\alpha = .90$). Total raw scores may range from 0 to 63. These scores are then converted into descriptive classifications based on cut-off scores: 0-13 is considered minimal range, 14-19 is mild, 20-28 is moderate, and 29- 63 is severe. (Beck Steer & Brown [3]).

Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire that assesses sleep quality and disturbances over a 1-month time interval. It has 19 items that generate 7 components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each com-

ponent is scored on a scale of 0–3 points where 0 indicates having “no difficulty” and 3 indicates having “severe difficulty” with sleeping. The seven components are then added to yield a total score that ranges 0–21 points. Higher scores indicate poorer sleep quality (Buysse Reynolds, Monk Berman & Kipfer [5]).

Fear of Missing Out Questionnaire (FoMO)

The FoMo Questionnaire is a 10-item questionnaire that uses a 5-point Likert scale where 1 is not true at all and 5 is extremely true. Scores are computed by averaging the scores across the ten items. Higher scores indicate a greater level of FoMO (Przybylski Murayama, DeHaan & Gladwell [15]).

Results

The present study examined the following hypotheses:

Hypothesis 1: Predicted that a positive relationship between cell phone addiction and Anxiety would be present.

Hypothesis 2: Predicted that there would be a positive relationship between cell phone addiction and Depression.

Hypothesis 3: Predicted that there would be a positive relationship between cell phone addiction and the fear of missing out (FoMO).

Hypothesis 4: there is a positive relationship between cell phone addiction and sleep issues.

We examined each hypothesis using correlational analysis, and the results were as follows:

Table 1. – Pearson's Correlations

Variable		Smartphone Addiction	Sleep	Depression	Anxiety	Fear of Missing Out
1	2	3	4	5	7	8
1. Smartphone Addiction	Pearson's r	–				
	p-value	–				
2. Sleep	Pearson's r	0.145	–			
	p-value	0.121	–			
3. Depression	Pearson's r	0.259**	0.393 ***	–		
	p-value	0.005	<.001	–		

1	2	3	4	5	7	8
4. Anxiety	Pearson's r	0.268**	0.260**	0.670***	–	
	p-value	0.004	0.005	<.001	–	
5. Fear of Missing Out	Pearson's r	0.344***	0.425***	0.505***	0.474***	–
	p-value	<.001	<.001	<.001	<.001	–

* $p < .05$, ** $p < .01$, *** $p < .001$

For hypothesis 1, we analyzed whether there is a correlation between smartphone addiction and anxiety. Based on the results of the study, there was a weak correlation between smartphone addiction and anxiety $r = .268, p = .004$.

For hypothesis 2, we analyzed whether there is a correlation between smartphone addiction and depression. Based on the results of the study, there was a weak correlation between smartphone addiction and depression $r = .259, p = .005$.

For hypothesis 3, we analyzed whether there is a correlation between smartphone addiction and FoMO. Based on the results of the study, there was

a significant correlation between smartphone addiction and FoMO $r = .344, p < .001$.

For hypothesis 4, we analyzed whether there is a correlation between smartphone addiction and sleep quality issues. Based on the results of the study, there was no correlation between smartphone addiction and sleep issues $r = .260, p = .121$.

Nevertheless, we also found a consecutive correlation among the variables through an exploratory analysis. The exploratory analysis was conducted to support the notion that smartphone use can subsequently affect a whole series of serious mental issues.

Table 2. – Pearson's Correlations

Variable		Smart-phone Use	Media Use	Smart-phone Ad-diction	Fear of Missing Out	Anxiety	Depres-sion	Sleep
1. Smartphone Use	Pearson's r	–						
	p-value	–						
2. Media Use	Pearson's r	0.432 ***	–					
	p-value	<.001	–					
3. Smartphone Addiction	Pearson's r	0.128	0.175	–				
	p-value	0.172	0.060	–				
4. Fear of Missing Out	Pearson's r	0.086	0.163	0.344 ***	–			
	p-value	0.358	0.080	<.001	–			
5. Anxiety	Pearson's r	0.109	0.010	0.268**	0.474 ***	–		
	p-value	0.244	0.916	0.004	<.001	–		
6. Depression	Pearson's r	0.078	-0.067	0.259**	0.505 ***	0.670 ***	–	
	p-value	0.404	0.473	0.005	<.001	<.001	–	
7. Sleep	Pearson's r	0.126	0.166	0.145	0.425 ***	0.260**	0.393 ***	–
	p-value	0.179	0.075	0.121	<.001	0.005	<.001	–

* $p < .05$. ** $p < .01$. *** $p < .001$

Through an exploratory correlational analysis, we found that smartphone use and media use are

moderately correlated, $r = .432, p < .001$. Media use is moderately related to smartphone addiction,

$r = .315, p < .001$. Smartphone addiction, then, is moderately related to the fear of missing out (FoMO), $r = .344, p < .001$. Then as the results showed, surprisingly, that FoMO shows significant correlation with anxiety $r = .474, p < .001$, depression $r = .505, p < .001$, and sleep $r = .425, p < .001$.

Discussion

This study intended to analyze whether smartphone use would have affected anxiety, depression, and sleep. Smartphone use is defined as students' usage of smartphones, which different levels could examine. The longer the smartphone usage, the greater risk of smartphone addiction. We examined smartphone addiction using SAS-SV. In this study, we operationally defined psychological well-being as anxiety, depression, FoMO, and sleep quality issues. Each specific well-being issue could be examined through its corresponding scale. Since mental disorders increase the risk for communicable and non-communicable diseases and contribute to unintentional and intentional injury, students are likely to be in a dangerous

situation even though they appear to have mild symptoms of mental well-being issues (Prince Patel, Saxena, Maj Maselko Phillips & Rahman [14]). In terms of the mental well-being disorders that we examined so far, smartphone addiction and overuse may be an influential factor in worsening them.

Conclusion

Overall, we hypothesized that smartphone use negatively affects people's psychological well-being. Based on the study results, hypotheses 1, 2, and 3 were supported and found that smartphone addiction correlates with anxiety, depression, and FoMO; however, the results of the study did not support hypothesis 4, in which there is no correlation between smartphone addiction and sleep issues. However, instead of the direct correlation between smartphone addiction and sleep issues, we found a consecutive relation between smartphone addiction, FoMO, and sleep issues. Based on (table 2), we found that smartphone use holds a relationship between a series of psychological issues.

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Section 5. Chemistry

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Kaize Yu,

Student, Beijing Huijia Private School, United States

E-mail: liliww2@gmail.com

AN EVALUATION OF A WASTEWATER RECLAMATION FACILITY EFFECTIVENESS

Abstract. Although reclaimed wastewater is typically not used for potable purposes, it can contain compounds which may pose risk to human health and the environment. This study investigated wastewater treated at a reclamation facility in Beijing, China. Semi-volatile organic compounds (SVOCs), including phthalate esters, polycyclic aromatic hydrocarbons, organochlorine pesticides, and nitrosamines, were analyzed from the influent, following biological treatment, and following final disinfection. The only compound found above the detection limit was diisobutyl phthalate, which was in the influent. No analytes were found above the detection limit in the remaining samples, indicating the treatment facility effectively removed diisobutyl phthalate from the wastewater.

Keywords: alternative water sources, wastewater treated, following biological treatment, disinfection.

1.0 Introduction

In many parts of the world, access to clean water is increasingly becoming a concern. Growing populations and accelerated industrialization have increased pressure on water security, which has led several countries to pursue alternative water sources (Yi et al. [11]). One common approach, especially in China's northern cities, is to improve the water utilization rate by reclaiming wastewater for irrigation, landscaping, recreation, and groundwater replenishment (Pinjing et al. [7]).

Reclaimed wastewater may contain hazardous compounds even following treatment. Trace compounds, including semi-volatile organic compounds (SVOCs) such as phthalate esters, polycyclic aromatic hydrocarbons, and organochlorine pesticides, may not be completely removed during the

treatment process (Garcia-Segura et al., [2]; Grandclement et al. [3]). Furthermore, chlorine disinfection processes generate disinfection byproducts such as nitrosamines (NAs) which can be carcinogenic (Liu and Zhong [5]; Fujioka et al., 2016). Although reclaimed wastewater is typically used as a non-potable source, there remains the risk of exposure to these compounds given the wide range and ubiquitous usage of reclaimed wastewater (Deng et al. [1]) evaluated the health risk of a wastewater reclamation facility's effluent SVOCs and NAs. The facility used an oxidation ditch, coagulation tank, biological aerated filtration, and ultraviolet disinfection to treat municipal wastewater. The authors found a potential risk of dermal exposure to polycyclic aromatic hydrocarbons, phthalate esters, and NAs exceeded the safety limit of 1×10^6 .

The present work investigated the influent and effluent from the Gaobeidian wastewater reclamation facility in Beijing, China. Sixty-six SVOCs, including organochlorine pesticides, phthalate esters, and polycyclic aromatic compounds, as well as four NAs were target analytes used to evaluate potential health risks from the treated effluent.

2.0 Material and methods

2.1 Wastewater treatment process

Samples were collected from a wastewater treatment facility in Beijing, China which received municipal wastewater. Effluent was used for cleaning roads and landscaping as well as being released to the Tong Hui River. The treatment process began with

coarse filtration and aerated sand settling (sedimentation). Next, wastewater entered a primary settling tank followed by an aeration tank in which activated sludge biologically removed contaminants. Nitrification also took place in the aeration tank to oxidize ammonia to nitrite and nitrate. Secondary sedimentation removed settleable materials and returned part of the sludge to the aeration tank. A denitrification process then converted nitrate to nitrogen gas. Membrane filtration completed the biological treatment. Disinfection then occurred via ozonation, ultraviolet irradiation, and chlorination before the effluent was discharged. Figure 1 provides a treatment process schematic as well as sampling point locations.

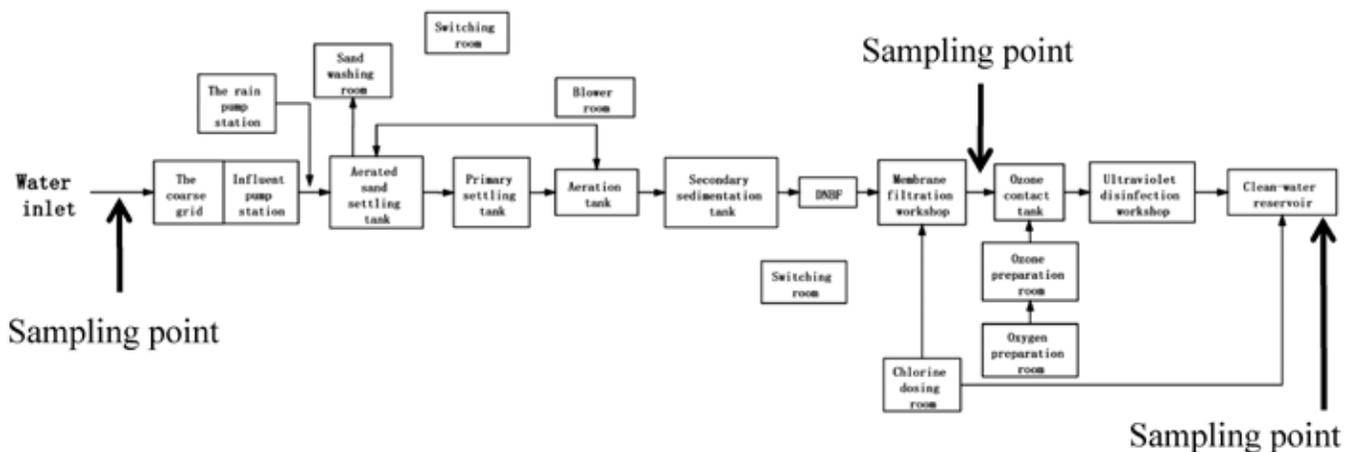


Figure 1. Wastewater treatment process schematic and sampling points

2.2. Wastewater sampling

Wastewater samples were collected from the wastewater influent, the membrane filtration effluent, and the final effluent. Sample points were chosen to evaluate the effectiveness of the overall biological treatment and disinfection processes. Samples were collected in two 5 mL amber glass bottles and a 10L bottle from each point. The two 5 mL samples enabled replication, and the 10L bottle provided a surplus of sampled wastewater if needed for additional testing. Budget constraints limited analyses to a total of three samples.

2.3. Analytical methods

SVOC target analytes included organochlorine pesticides, phthalate esters, polycyclic aromatic

compounds, and other SVOCs. NAs were analyzed as well. Centre Testing International Group Beijing Co., Ltd., a certified commercial laboratory, performed the sample preparations and analyses. The nine organochlorine pesticides were analyzed using US Environmental Agency (EPA) Method 8081B (EPA [9]) using gas chromatography and an electron capture detector or electrolytic conductivity detector. Five of the phthalate esters were analyzed using ISO Standard 18856:2004 (ISO [4]). The remaining phthalate esters, polycyclic aromatic hydrocarbons, NAs, and other SVOCs samples were prepared by separatory funnel liquid-liquid extraction with EPA Method 3510C (EPA [8]) and analyzed

by gas chromatography/mass spectrometry with EPA Method 8270E (EPA [10]).

3. Results and discussion

3.1. SVOC and NA concentrations

Table 1 lists the analytes, their compound category, analytical method, and concentration in the

influent, following membrane filtration, and the final effluent. Only one compound, diisobutyl phthalate, was measured above the detection limit in the influent at 3.25×10^{-3} mg/L (highlighted in table). The remaining samples and analytes were all below the detection limits.

Table 1.– Sample results

Analyte	Compound category ¹	Analytical method	Influent (mg/L)	Membrane filtration(mg/L)	Effluent (mg/L)
1	2	3	4	5	6
1-Naphthylamine	NA	EPA 8270E	$< 9 \times 10^{-4}$	$< 9 \times 10^{-4}$	$< 9 \times 10^{-4}$
4-Nitrobenzenamine	NA	EPA 8270E	$< 7 \times 10^{-4}$	$< 7 \times 10^{-4}$	$< 7 \times 10^{-4}$
N-nitroso diphenylamine	NA	EPA 8270E	< 0.010	< 0.010	< 0.010
N-Nitrosodi-n-propylamine	NA	EPA 8270E	< 0.010	< 0.010	< 0.010
N-Nitrosodimethylamine	NA	EPA 8270E	$< 2 \times 10^{-3}$	$< 2 \times 10^{-3}$	$< 2 \times 10^{-3}$
BHC (total)	OP	EPA 8081	$< 4 \times 10^{-4}$	$< 4 \times 10^{-4}$	$< 4 \times 10^{-4}$
Aldrin	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
DDT (total)	OP	EPA 8081	$< 4 \times 10^{-4}$	$< 4 \times 10^{-4}$	$< 4 \times 10^{-4}$
Dieldrin	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
Endosulfan- II	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
Endosulfan-I	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
Endrin	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
Heptachlor	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
Heptachlor epoxide	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
o, p'-DDT	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
p, p'-DDD	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
p, p'-DDE	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
p, p'-DDT	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
α -BHC	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
β -BHC	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
γ - BHC	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
δ - BHC	OP	EPA 8081	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$
1-Chloro-4-phenoxybenzene	Other SVOC	EPA 8270E	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$
1,2-Dichlorobenzene	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
1,2,4-trichlorobenzene	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
1,2,4,5-Tetrachlorobenzene	Other SVOC	EPA 8270E	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$
1,3-Dichlorbenzene	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
1,3-Dinitrobenzene	Other SVOC	EPA 8270E	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$

1	2	3	4	5	6
1,3,5-Trinitrobenzene	Other SVOC	EPA 8270E	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$
1,4-Dichlorobenzene	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
2,4-Dinitrotoluene	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
2,6-Dinitrotoluene	Other SVOC	EPA 8270E	$< 5.7 \times 10^{-3}$	$< 5.7 \times 10^{-3}$	$< 5.7 \times 10^{-3}$
3-Nitroaniline	Other SVOC	EPA 8270E	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$
4-Bromodiphenyl ether	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
4-Chloroaniline	Other SVOC	EPA 8270E	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$
4,4'-Diaminobiphenyl	Other SVOC	EPA 8270E	$< 8 \times 10^{-4}$	$< 8 \times 10^{-4}$	$< 8 \times 10^{-4}$
Aminoazobenzol	Other SVOC	EPA 8270E	$< 9 \times 10^{-4}$	$< 9 \times 10^{-4}$	$< 9 \times 10^{-4}$
Dibenzofuran	Other SVOC	EPA 8270E	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$	$< 5 \times 10^{-3}$
Hexachlorobenzene	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
Hexachlorobutadiene	Other SVOC	EPA 8270E	$< 9 \times 10^{-4}$	$< 9 \times 10^{-4}$	$< 9 \times 10^{-4}$
Hexachlorocyclopentadiene	Other SVOC	EPA 8270E	$< 2 \times 10^{-3}$	$< 2 \times 10^{-3}$	$< 2 \times 10^{-3}$
Hexachloroethane	Other SVOC	EPA 8270E	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$
Isophorone	Other SVOC	EPA 8270E	$< 2.2 \times 10^{-3}$	$< 2.2 \times 10^{-3}$	$< 2.2 \times 10^{-3}$
Nitrobenzene	Other SVOC	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
Butyl benzyl phthalate	PAE	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Di(undecyl) phthalate	PAE	ISO 18856	$< 5 \times 10^{-6}$	$< 5 \times 10^{-6}$	$< 5 \times 10^{-6}$
Dibutyl phthalate	PAE	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Dicyclohexyl phthalate	PAE	ISO 18856	$< 4 \times 10^{-6}$	$< 4 \times 10^{-6}$	$< 4 \times 10^{-6}$
Didecyl phthalate	PAE	ISO 18856	$< 5 \times 10^{-6}$	$< 5 \times 10^{-6}$	$< 5 \times 10^{-6}$
Diethyl phthalate	PAE	EPA 8270E	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$
Diisobutyl phthalate	PAE	ISO 18856	3.25×10^{-3}	$< 4 \times 10^{-6}$	$< 4 \times 10^{-6}$
Dimethyl phthalate	PAE	EPA 8270E	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$
Dioctyl phthalate	PAE	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Dioctyl phthalate	PAE	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Dipropyl phthalate	PAE	ISO 18856	$< 5 \times 10^{-6}$	$< 5 \times 10^{-6}$	$< 5 \times 10^{-6}$

1	2	3	4	5	6
2-Chloronaphthalene	PAH	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$
Acenaphthene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Acenaphthylene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Anthracene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Benz(a)anthracene	PAH	EPA 8270E	$< 7.8 \times 10^{-3}$	$< 7.8 \times 10^{-3}$	$< 7.8 \times 10^{-3}$
Benzo[a]pyrene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Benzo[b]fluorathene	PAH	EPA 8270E	$< 4.8 \times 10^{-3}$	$< 4.8 \times 10^{-3}$	$< 4.8 \times 10^{-3}$
Benzo[ghi]perylene	PAH	EPA 8270E	$< 2 \times 10^{-3}$	$< 2 \times 10^{-3}$	$< 2 \times 10^{-3}$
Benzo[k]fluoranthene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Chrysene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Dibenzo[ah]anthracene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Fluoranthene	PAH	EPA 8270E	$< 2.2 \times 10^{-3}$	$< 2.2 \times 10^{-3}$	$< 2.2 \times 10^{-3}$
Fluorene	PAH	EPA 8270E	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$
Indeno[1,2,3-cd]pyrene	PAH	EPA 8270E	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$	$< 2.5 \times 10^{-3}$
Naphthalene	PAH	EPA 8270E	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$	$< 1.6 \times 10^{-3}$
Phenanthrene	PAH	EPA 8270E	$< 5.4 \times 10^{-3}$	$< 5.4 \times 10^{-3}$	$< 5.4 \times 10^{-3}$
Pyrene	PAH	EPA 8270E	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$	$< 1.9 \times 10^{-3}$

¹OP = organochlorine pesticide, NA = nitrosamine, PAE = phthalate ester, PAH = polycyclic aromatic hydrocarbon

3.2 Detected compound

The only compound detected in the influent was diisobutyl phthalate ($C_{16}H_{22}O_4$), which is used as plasticizer to aid the process of making plastic softer and flexible. Although this phthalate ester and diester is a teratogenic agent and peroxisome proliferator-activated receptor modulator, its toxicity is considered low. It is also flammable and non-volatile. This compound is soluble in resin but not water (National Library of Medicine [6]). The presence of this substance in the influent suggests that industrial wastewater using this compound may have been sent to the facility. However, the concentration in the influent was relatively low and was removed to below the detection limit in the samples following biological treatment and disinfection. Therefore, the analytes pose no known risk of harm to humans or the environment from the reclaimed wastewater.

It is important to note that budget constraints limited analyses to a total of three samples, with a single sample collected from three sample points. Thus, the results lack statistical power, and the conclusions must be caveated as such. The study also did not reveal

which biological treatment process was responsible for removing the diisobutyl phthalate from the wastewater. Future work should investigate additional sampling points with multiple replicate samples to provide statistically defensible results and elucidate which treatment component removes the contaminant.

4. Conclusions

SVOCs or NAs were analyzed from a wastewater reclamation facility in the influent, following biological treatment, and following disinfection. The only compound found above the detection limit was diisobutyl phthalate, a common chemical used as plasticizer. No analytes were found above the detection limit in the remaining samples, indicating the treatment facility effectively removed diisobutyl phthalate from the wastewater. However, the results lacked statistical power since only one sample was collected from each of three sample points. Future work should investigate additional sampling points with multiple replicate samples to provide statistically defensible results and determine which treatment component removes the contaminant from the wastewater.

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Section 6. Economics and management

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Wenfeng Shi,

Student in High School, Kent School, U.S.

E-mail: shiw22@kent-school.edu

COVID-19 IMPACT ON THE WORLD

Abstract. This research is conducted to find how COVID and the result of the pandemic affected the world economy especially the U.S. economy mainly from mid-2020 to mid-2021. After the pandemic hit, the U.S. economy has turned into stagnant water. The pandemic has clearly affected the U.S. economy and to the point where the presidential administrations and the Federal Reserve had to release many stimulus bills that help the U.S. economy. I researched the U.S. GDP, COVID cases, COVID mortality rate, and more from data that was found in the government and other websites, and compared them to complete my analysis. Several graphs were provided to further prove the thesis. I also researched a particular industry – the automobile industry. The automobile industry was greatly affected by the pandemic and they are recovering from the hit. The major point was that the U.S. and world economy has been greatly affected by the pandemic, and through the numbers, the GDP growth rate has lowered during the mid-2020 to mid-2021. The economy, however, is going in an upward trend right now through the stimulus bills and fewer worries on COVID itself. Both the stock market and the GDP growth rate have proved that the U.S. economy is recovering at a historically fast pace, and there shall be no worries about it.

Keywords: COVID, pandemic, world economy, economic recession, automobile industry, stimulus bills.

Introduction

COVID-19, a disease that has absolutely horrendous for the world. It is spread through air and surface, so it is really hard to prevent and easy to catch. The disease has forced many of us to wear a mask while walking outside, and staying the social distance between each of us. The number of cases of COVID is high in the United States, reaching a high of 6.43 million cases in one month, with the highest mortality rate per case being 6.13% in one month. This disease has also brought fear in the world, the fear to catch the disease and eventually die from it. This disease is unfriendly

to the elders above age 65, and very young children. The mortality rate is absurdly high to the point where people are less likely go out and meet each other. They have to restrain themselves inside a room, and it's not one of the best feelings that a person would get. The COVID pandemic also hurt the economy. In the United States, the economy has hit the rock bottom since 2008. With people less willing to go outside and spend, the GDP drastically went down in the second quarter of 2020, almost down by 30%. Small businesses were hurt the most during the pandemic, because people are less willing to go out and spend. Unemployment

rate went to 14.8% in April of 2020, which means that almost 1 in 7 Americans in April of 2020 were without a job. However, the government has helped the economy to cover relatively soon. Trump issued plans to help the American household, with money given out every week to the qualified family. The banks lowered its interest rates, which helped people to borrow more and more, and helping people to invest, which helped the stock market in a sense. The economy has bounced back with many moves made by Trump. In the third quarter of 2020, the economy grew by almost 30%, which offsets the lost in the economy in the second quarter of 2020. With all the money sent out from the government, the inflation rate also rose, however the chair of Federal Reserve, Jerome Powell, believes that it will not affect the inflation rate in the long term. The Federal Reserve believes that they can control the inflation rate around 2% as targeted. This gives a positive sign to the American economy, and calms the nerves of many American citizens. Later, as Biden was inaugurated, he put a lot of work on controlling the pandemic. He wanted the country to be on pace for 1 million doses of vaccines per day, which was successfully, with some days reaching higher than 1.5 million

doses of vaccines per day. The vaccines would allow people to have confidence to go out and spend more. Furthermore, he signed one of the biggest stimulus bills – The American Rescue Plan. The most important part of The American Rescue Plan is the \$1.9 trillion COVID-19 Stimulus Plan. This plan would allow the qualified citizens to get \$1400 per person, which they could choose to either save it or spend it. The marginal propensity to consume for each income quintile from high to low is 0.55, 0.40, 0.22, 0.13, 0.12 respectively. Since the \$1400 would help the mid to lower class the most, we will take 0.13 into calculation for the spending multiplier. The \$1400 aid would convert to a value of around \$1609.2 in the economy, and this would also make the \$1.9 trillion package be worth at least \$2.18 trillion for the economy. These are some great sign for the American economy, and gives the American citizens a confidence boost. The American government has done a relatively fine job fighting the disease and the recession, and the economy is going relatively well, especially the stock market. These positive signs would signal that the United States has gotten out of the recession with a really good position economically.

GDP & Unemployment affected by COVID

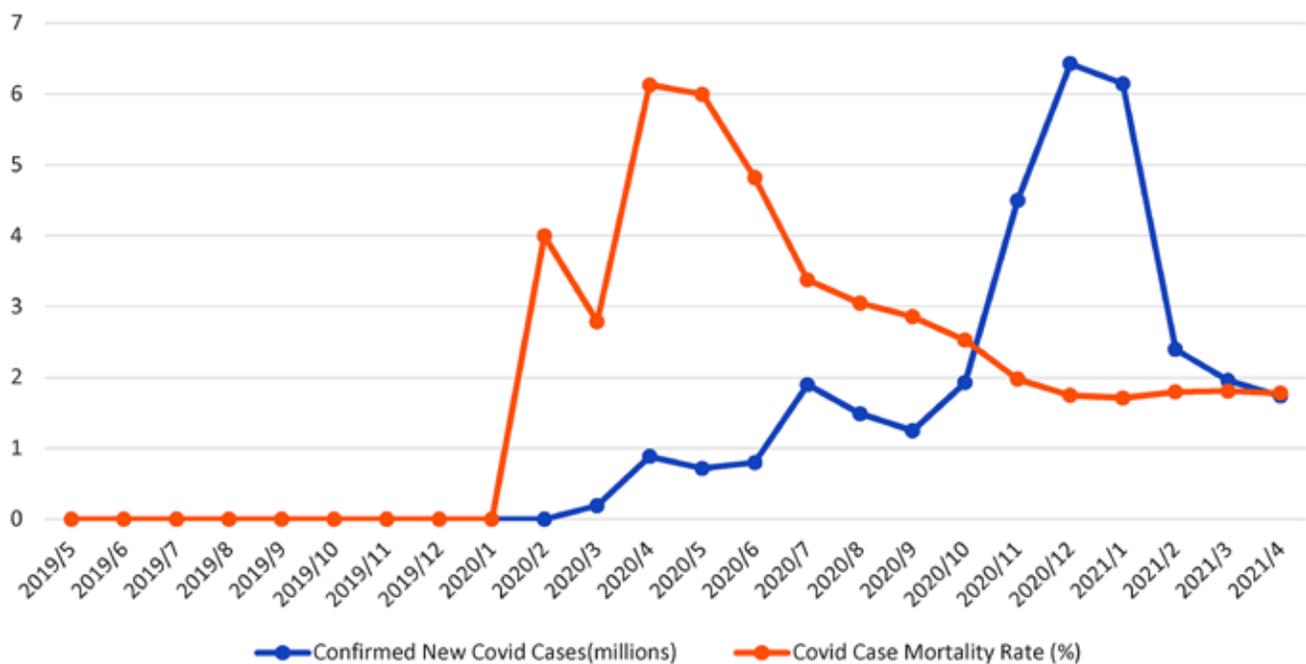


Figure 1. Confirmed New COVID Cases (millions) vs. COVID Case Mortality Rate (%)

The graph above has shown how the COVID has developed over the past year. In January, the first COVID case occurred, and since the COVID case has been grown until July. Later in October to December we see a huge rise in the number of new cases confirmed, and has been easing off ever since. When COVID first hit, the country was in lockdown and the economy was shutdown. It was no good news for the United States. Before the pandemic hit, the GDP growth was at a very high rate, growing around 0.3–0.4% per month. Most Americans were satisfied with their lives. The country was growing as a whole. The high amount of GDP growth would mean that

people are living better and better off. This is what the U.S. government wanted to see. Americans were satisfied with the government, and this would ultimately form a virtuous cycle in the United States between the politics part and the citizens part. However, at 2020, as mentioned before, COVID hit. Why does COVID have to associate with the economy? One might ask. The answer is not complicated. The reason is that since people are forced to stay home to prevent the spread of the COVID virus, people are unable to spend at their local grocery stores, restaurants, malls, etc. Their inability to spend would cause the economy to be in a recession.

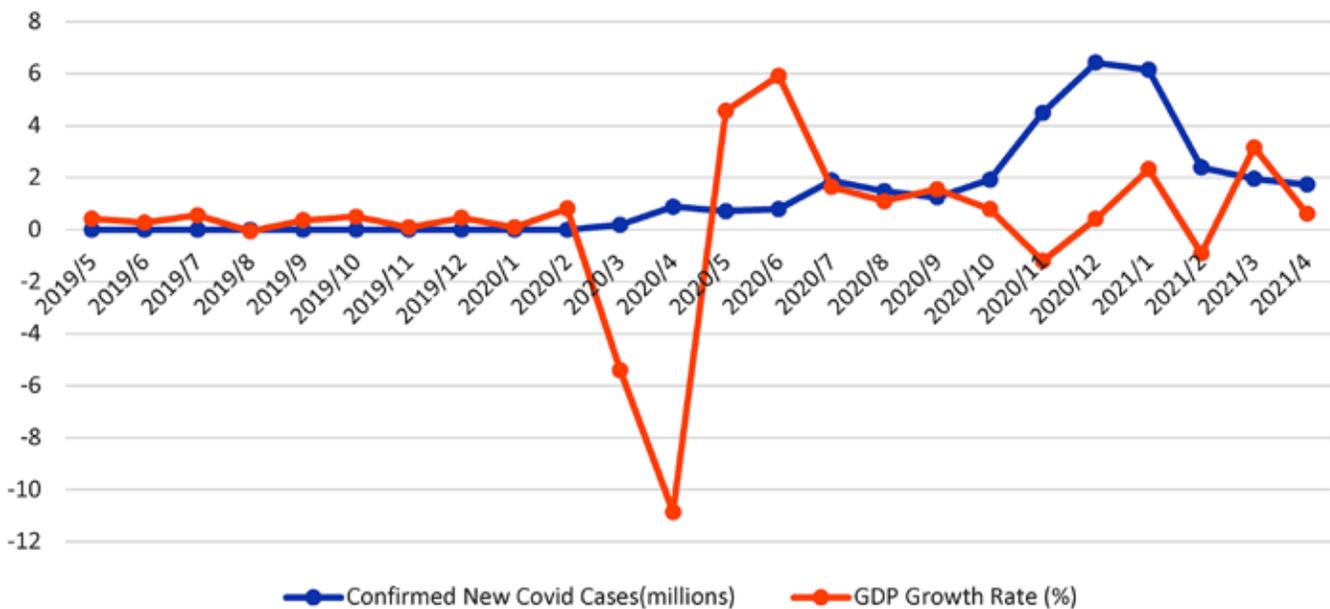


Figure 2. Confirmed new COVID Cases (millions) vs. GDP Growth Rate(%)

In the graph above, blue line stands for the confirmed new COVID cases each month since May of 2019, and the orange line stands for the GDP growth rate for each month since May of 2019. As you can see, in April, when the new COVID cases started to rise, the GDP growth rate went to a horrendous -10.85% . That is a huge hole in the GDP growth rate. In this graph, it can clearly tell that the GDP growth rate is related to the COVID-19 cases. In April, when COVID was spreading at a relatively high pace at the time, people refused to go out. People would spend less, and others would earn less,

so others would spend less... this is ultimately a vicious cycle which no one wants to see. The local stores, where a lot of Americans would work at, were forced to shut down. Many Americans were left without a job, and their ability to spend has been at its worst. People started to struggle to pay for their rents, food, and other daily utilities. People are struggling for life for sure. And the American government was doing its best to prevent it. With people losing more and more jobs, the unemployment went to 14%, a really high number that hasn't been seen in years.

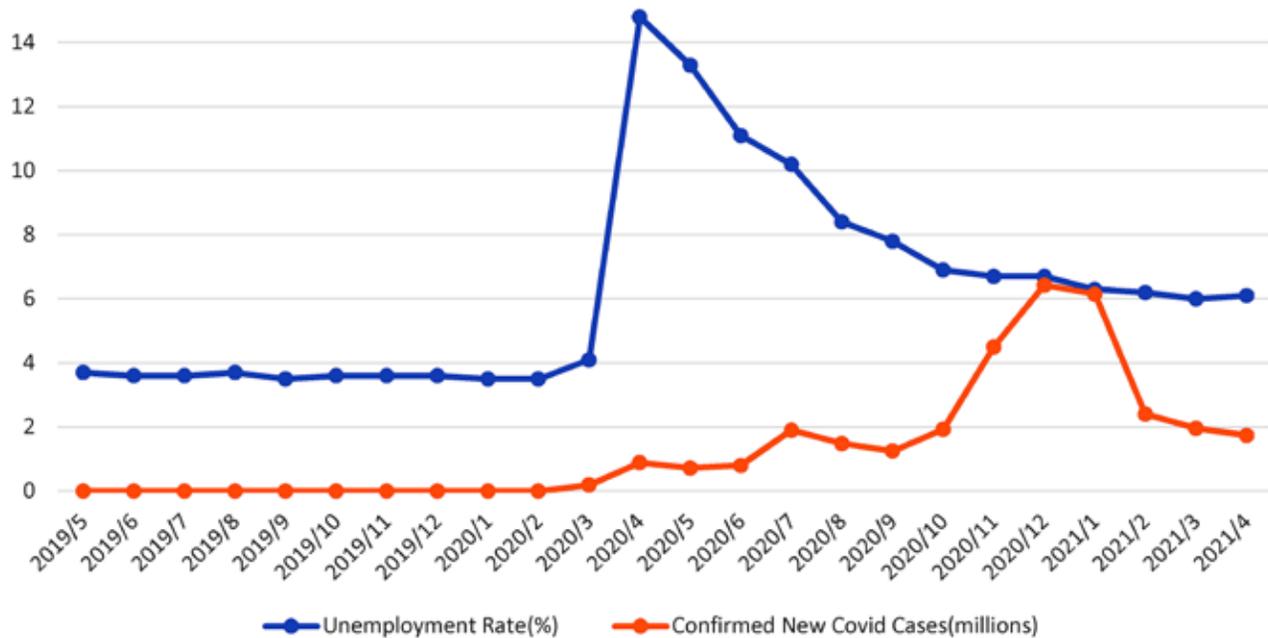


Figure 3. Unemployment Rate (%) vs. Confirmed New COVID Cases (Millions)

The unemployment rate is a good indicator of how much the Americans were struggling. The unemployment rate and GDP are ultimately just two numbers, but the living standards of the Americans were the GDP and unemployment rate ultimately indicate, and the numbers weren't looking so lively. You can clearly see that from October to December, when the numbers of confirmed new COVID cases has bounced back, the unemployment also went up by a little bit, following the trends of when new confirmed COVID cases are high, the unemployment and GDP is supposed to be low. The reason might be that Americans refuse to work during when the COVID case number is high. From October to December, the COVID vaccine has yet to be speeded out in a vast amount of numbers, so the employees, many of whom has young children or elders adults in their family, wouldn't the risk of catching COVID and passing it on to the more dangerous group. In the COVID death rate studies, young children and elder adults are the groups that will experience the highest risk of dying when they catch COVID. Clearly the employees would not want to risk the chance of them having a life threaten disease, rather to take

the rescue plans sent by the government, and live through the short tough amount of period. Though the GDP growth rate was going at the right direction from October to December, we may believe that the holiday maybe one great influencer of the GDP. In October, there is Halloween. In November, there is Thanksgiving. In December, there is Christmas. The three holidays are extremely important to the American households, which also helped to explain why the COVID cases went up. Since the family are more willing to travel during holidays, the COVID cases went up because more and more people are going outside, and therefore has a higher chance of getting COVID. However, while they are outside, they are able to spend at the local restaurants, stores, etc., which helped the economy at a great scale. This explains the outbreak of the number of new COVID cases and also the high growth rate from October to December. However, spending in the local restaurants, stores would help the local economy to run, and those stores and restaurants would be able to pay for more employees and lower the unemployment rate. Also, it would help the economy because of the multiplier effect, which would mean that the

amount of dollars the traveler spent would turn into an amount that is much more than the original

amount in the economy, and that is what the American economy is lacking during the pandemic.

Table 1. – Pre-Pandemic vs. During Pandemic

	Pre-Pandemic (Average)	During Pandemic (Average)
GDP Growth Rate (%)	0.34	0.29
Unemployment Rate (%)	3.68	7.6
New COVID Cases (Millions)	0	2.02
Case Fatality Rate (%)	0	2.9

The table above is a table that contains the Pre-Pandemic numbers and the During Pandemic numbers. The GDP growth rate went down from 0.34% per month to 0.29% per month. The unemployment rate went up from 3.68% to 7.6%, a huge jump, doubling the unemployment numbers. The average of the new COVID cases per month is a scary 2.02 million cases. The case fatality rate is 2.9%, which is not horrible for the American community. This table's numbers show

how much the pandemic has affected the American people's lives. The scary 7.6% unemployment rate is only the average, the high is at 14.8%, which is a horrible news. However, the government issued recovery bills which gives the unemployed people just enough money for them to live through this pandemic, and successfully find a job. By the end of April 2021, the government has successfully lowered the number to 6.1%, which is 8.7% less than the peak.



Figure 4. S&P 500 During the Pandemic

Stock Market is another part of the economy that has taken a huge hit. The figure below is a graph of the S & P 500 index during the pandemic. As one

could see on the graph, the index's value has quickly dropped during March, which is when the pandemic has started. And the stock market has gone through

multiple trading curbs during that period of time. The stock market is a good indicator of economy and the S & P 500 is a good indicator of the stock market, as it is composed of multiple big-name stocks in the market. With the stock market struggling early on during the pandemic, it could be almost certain that the U.S. economy was going through a hardship. However, the stock market bounced back eventually with the help of many COVID relief packets from the government. Now the stock market is skyrocketing and increasing at a very high rate.

The COVID has affected many Americans' lives, but the spread of the vaccine will help the American households, giving them the confidence to go outside, and possibly spend more. The American Rescue Plan by Biden and the recovery plan by Trump has helped the American economy by a great scale, especially reflecting in the stock market,

which is absolutely booming. With the money that Americans receive from the Rescue Plan, they have money they don't know where to put, so they put it in the stock market, since the demand goes up, the price of the stocks has gone up. This is a good indicator that the United States is in a recovering stage, and Americans do not need to worry about the economy too much in the near future.

Automobile Industry

The automobile industry is consisted mostly by the cars in the world. The market size in the U.S. in 2021 is \$82.6 billion. The value of the global market is around \$2.7 trillion. The market in the U.S. grew 12.6% in 2021, mostly due to the sudden hit in 2020 due to the pandemic, which lead the automobile industry to hit the rock bottom of it. Some of the biggest brands in the industry are BMW, Mercedes-Benz, Toyota, Honda, Audi, Volkswagen, etc.

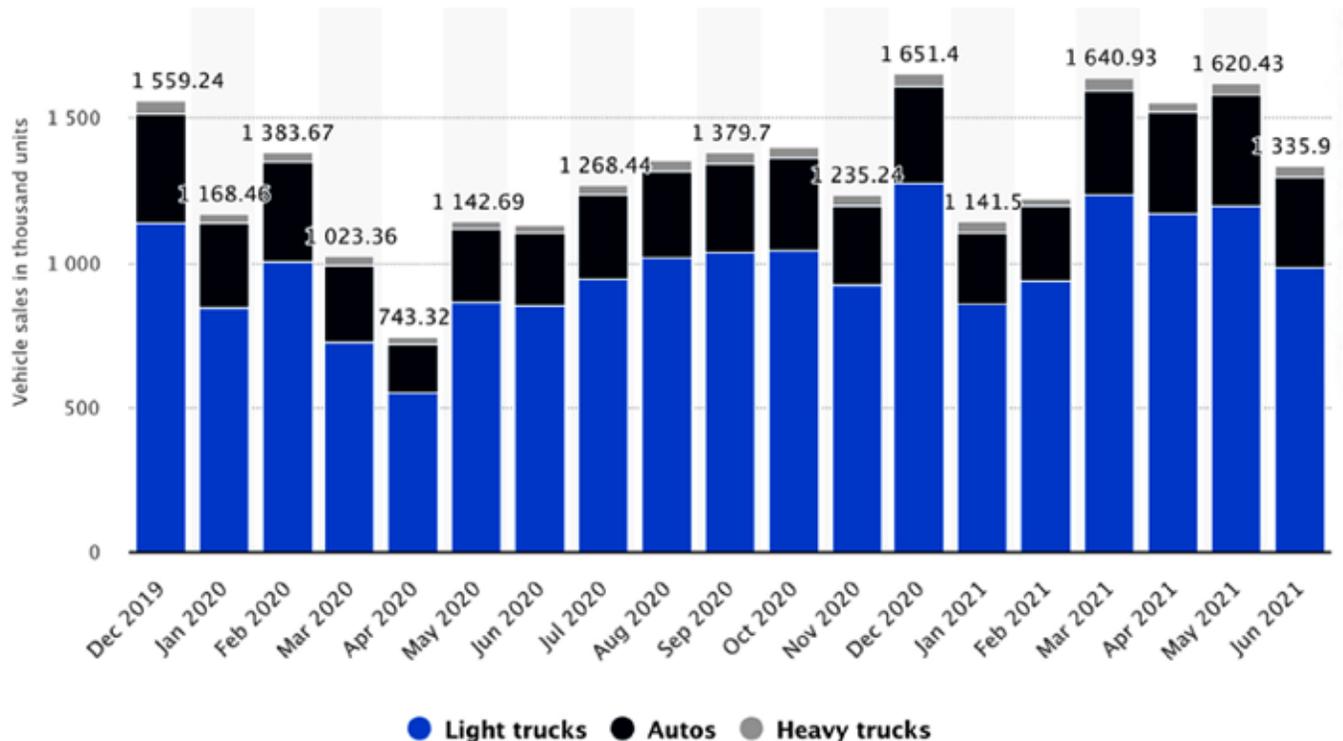


Figure 5. Vehicle Sales (thousands)

The automobile is one of the industries that has been affected largely due to the pandemic. In June of 2020, the manufacturing employees was 20,000

less than it is in 2021. The dealership employees are about 100,000 down. The total employed in the industry in April 2021 is also 1 million more than

the total employed in April 2020. These numbers have indicated that the automobile industry has been truly hit by the pandemic, and it is still not recovering to its fullest. The number of cars sold has also gone down significantly during the pandemic. As one could see on the graph below, the sales were at the normal rate at December 2020 to February 2020, but the sells number significantly dropped in March and hitting a rock bottom in April 2020. This fits well with the pandemic line, as the shutdown was implemented in March and April. When the United States were trying their best to prevent the

spread of the virus, which was in March and April, people did not go out and many people were finding themselves without a job. This would significantly hurt the purchase ability of many Americans, which explains the lack of purchase in March and April. When the U.S. finally opened itself up and with many COVID relief plans, the purchase power went right back up and the sales of cars went to the same level as the pre-pandemic level.

The stock market of the car manufacturers is also a good indicator of the car manufacturing companies in 2020.

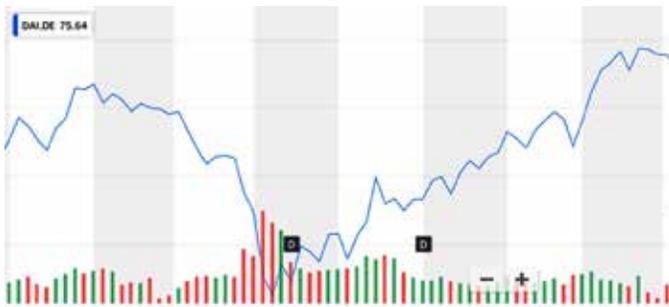


Figure 6. Stock of Daimler during the Pandemic

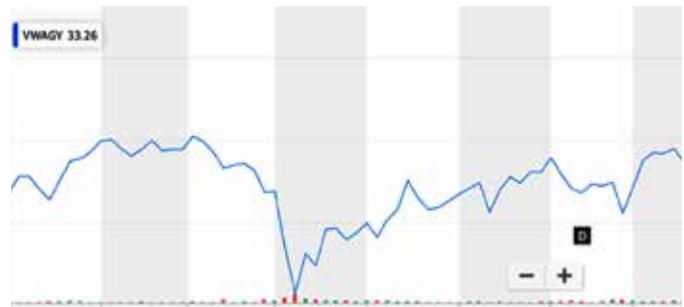


Figure 7. Stock of Volkswagen During the Pandemic



Figure 8. Stock of BMW During the Pandemic



Figure 9. Stock of GM During the Pandemic

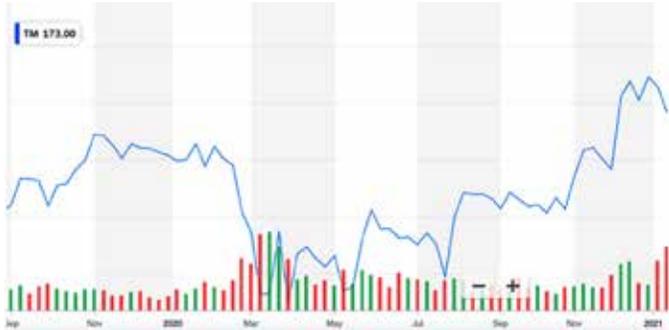


Figure 10. Stock of Toyota During the Pandemic



Figure 11. S&P500 During the Pandemic

Here is the stock market chart from five of the biggest cars manufactures in the world from September 2019 to early 2021. The five tycoons are: Daimler, BMW, Volkswagen, General Motors, and Toyota. The last chart is the chart of the S & P 500 index. The stock of the five cars manufactures have generally went along the lines of the S & P 500 index. The stock price of most of the car manufactures are going upwards or in a stable stage before the pandemic in March, and all of them had a huge drop in March, which was due to the pandemic. And after the pandemic has hit, most of the stock prices are on a rise, which fits well with the recovering stage after the recession. The stock market has clearly showed that the five tycoons were victims of the pandemic, and that the automotive industry has taken a hit due to the pandemic.

The revenues of each of the cars manufactures have also went down due to the pandemic. The Daimler AG, the parent company of the famous Mercedes-Benz, has saw the revenue going down 17 billion USD in 2020 comparing to 2019. Volkswagen AG, the parent company of Volkswagen, Bentley, Lamborghini, Audi, etc., has saw the revenue going down almost 30 billion USD in 2020 comparing to 2019. General Motors' revenue went down around 15 billion. Toyota motors, however, saw the revenue actually going upwards, from 272 billion USD to 275 billion USD. BMW saw itself going down 6 billion USD in 2020 comparing to 2019. The revenues of the five tycoons, with the exception of Toyota Motors, have all went down in 2020, which is a good indication that the COVID recession has truly hurt the automotive industry.

Conclusion

Clearly, the pandemic has hit really hard not only on the people, but also on the economy. As stated throughout the paper, the pandemic has hit the economy in the ways of low spending, unemployment, small business owners losing their businesses, and more. Nobody wants to experience this sort of economic recession, but economic recession is a part of the economic cycle and it almost always have to be dealt with. Many economists had the belief that if the 2020

economic recession did not happen, the U.S. would eventually face another one in 2022. The pandemic has truly hurt the mid to bottom of the U.S. population the most, while the richest' wealth grew, the mid to bottom of the U.S. was suffering. They were facing problems with paying rents, affording their daily spending, as quite a number of them was cut in due to the economic recession. Small and local businesses owners could not stay open because there was simply nobody who was going out and spend, and most people decided to cut their spending down to the necessities, so they did not have the luxury to go to the local restaurants to dine or to go out and buy items from the local businesses. Many people had their darkest days of their lives during the pandemic, due to that they just could not afford to live. The stock markets were doing horrendous at that time, and many people lost their life savings in the stock market. This brought many anxiety and depression across the U.S. The Federal Reserve was releasing little to no interests to banks to try to loan money out to people and get them to spend more. This seemed like a desperate attempt from the Federal Reserve.

Luckily, now in 2021, the hit of the pandemic has seemingly pass by. With the COVID relief bills and even more help from the central government, the U.S. economy has recovered. The stocks are even hitting new highs after the pandemic. Under the Biden Administration, the COVID vaccine has kicked into effect and boosted the travel back to life. With restaurants, hotels, even stadiums opening again, people in the U.S. could see entertainment and travel in real life instead of just browsing YouTube online. People are not mandated to wear masks with certain restrictions, schools are opened again, and many people are vaccinated so that they will not be living in the shadow of the virus. Even though the Delta variant has hit again, but it is believed that the COVID vaccines has an effect on the COVID Delta variant so that even if the patient catches the variant, the patient's chance of having a horrible sickness would be lowered by a large margin. With local family owned

businesses opening, the economy of the mid to lower class could really enjoy the revival of their revenues. Sports events is able to open to public again, with kids playing in the Little League Worlds Series to professionals who has been finding ways to play sports under the pandemic. MLB NBA, NFL, and more leagues are enjoying a great number of viewers not only online, but also in the ball parks and stadiums. People could really hear the cheers again, and it is demonstrated in many NBA games. The careers of many players are allowed to be continued, and could really go out and enjoy games at the high-

est level possible. With the revival of the economy, the unemployment level has gone down significantly, with is what the Federal Reserve has been scratching their heads about ever since the pandemic has started. With the lower unemployment, more people could earn money, which means that more people could go out and spend, which would result to better economy, reviving the virtuous cycle that has been going on before the pandemic. With still many cases every day, many people feel that the pandemic has been almost over in the U. S. Many people are able to return to their lives before pandemic.

Glossary

GDP – gross domestic product;

Unemployment rate – the proportion of unemployed people;

Inflation rate – the rate at which the value of a currency is falling and level of prices for goods and services is rising;

Economic Recession – a period of declining economic performance across an entire economy that lasts for several months;

American Rescue Plan – plan passed to provide people who need money during the pandemic;

GDP Growth Rate – rate at which the GDP is growing;

Pandemic – Referring to the COVID Pandemic;

Stock Market – a stock exchange;

Recovery Bills – referring to the acts passed to help people who need money during the pandemic;

S&P 500 – a market-capitalization-weighted index of 500 leading publicly traded companies in the U.S.;

Revenue – income of a company.

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