ECONOMIC BURDEN OF INFLUENZA-LIKE ILLNESS STUDY IN MONGOLIA 2021–22

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ECONOMIC BURDEN OF INFLUENZA-LIKE ILLNESS STUDY IN MONGOLIA 2021-22

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Tsogt Mend

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This certifies that the Master's Thesis

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DECLARATION

I, Tsogt Mend, hereby declare that the research **"Economic Burden of Influenza Like Illness Study in Mongolia, 2021-22"** is submitted as a thesis for the competition of my Master's Degree of Health Policy and Financing Capacity Building Program at Yonsei University, Seoul. It is the full results of my investigation; all ideas, references, and content have been acknowledged. I also certify the results of this study have not been submitted in any degree and neither are currently submitted to a candidate of any degree.

Tsogt Mend

Seoul, 23rd November 2022

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LIST OF ABBREVIATIONS

BoD	Burden of Disease
CI	Confidence Interval
COI	Cost of Illness
CT	Computer Tomography
DRG	Diagnostic Related Groups
ICD-10	International Classification of Diseases 10
ILI	Influenza Like Illness
LMIC	Low- and Middle-Income Countries
MNT	Mongolian Tugrik
MoH	Ministry of Health
MRI	Magnetic Resonance Imaging
NBS	National Bureau of Statistics
NHI	National Health Insurance
NITAG	National Immunization Technical Advisory Group
OOP	Out Of Pocket
RT-PCR	Real-Time reverse transcription Polymerase Chain Reaction
SAGE	Strategic Advisory Group of Experts
SARI	Severe Acute Respiratory Infection
USD	United States Dollar
WHO	World Health Organization
RSV	Respiratory Syncytial Virus

ABSTRACT

Seasonal influenza is one of the major public health threats to humans causing morbidity and mortality. Approximately 1280 influenza-like illness (ILI) and 140 Severe Acute Respiratory Infection (SARI) cases per 10,000 population get reported through sentinel surveillance in Mongolia. The evidence of the OOP and economic burden of ILI among risk groups (children below 5 years old, pregnant women, and older adults) is not clearly defined. We aimed to determine the economic burden on the population. This is a cost-of-illness study presenting findings as per episode. The WHO Manual is used to adapt questionnaires, analyze data, and present data from the societal perspective. A total of 2779 participants agreed to participate in the study. Amongst the participants, 1227 (44.2%) were children below 5 years old, 778 (28.0%) were people above 65 years, and 774 (27.9%) were pregnant women. Therefore, 1044 (38.1%) participants were hospitalized owing to SARI, and 1703 (61.9%) were outpatients at health centers. The ILI per episode cost was 19.65 (18.53 – 20.77) USD and 31.73 (29.20 – 34.26) USD in SARI episodes. The annual costs based on the per episode costs for ILI/SARI visits reported at the sentinel sites were approximately 11 million USD (10,9 mln – 11,5 mln) from ILI episodes and 2.8 million USD (2.6 mln – 3 mln) from SARI episodes. Despite the population impact, children below 5 years old had the highest direct cost and pregnant women had the highest indirect cost compared with the other risk groups. The economic burden of the illness affected low-income households adversely. Furthermore, near-poverty-class households were experiencing catastrophic healthcare costs owing to ILI and SARI episodes. These results will be used as part of the evidence to further study the cost-effectiveness of seasonal influenza in Mongolia to improve vaccination uptake and increase awareness of ILI/SARI prevention and treatment.

Keywords: cost-of-illness, the economic burden of influenza, seasonal influenza

I. INTRODUCTION

Background

Seasonal influenza is one of the major public health threats to humans causing morbidity and mortality. The World Health Organization (WHO) estimated that 250,000–500,000 deaths annually are caused by influenza (WHO, 2022). Mongolia is among the countries where seasonal influenza and influenza-like illness (ILI) have a clear seasonal pattern. Approximately 1280 ILI and 140 Severe Acute Respiratory Infection (SARI) cases per 10,000 population get reported through sentinel surveillance in Mongolia (NIC Mongolia, 2022). Therefore, the cold season starts with other respiratory pathogens including RSV, Rhinovirus, Adenovirus, and so on, and these pathogens are accountable for approximately 40% of ILI and SARI admissions each season.

We have estimated the economic burden of seasonal influenza in 2018/19, and outpatient visit costs were catastrophic for households with lower incomes. ILI has a high socio-economic impact that affects the whole population. For instance, if ILI and SARI per 10,000 population exceed a certain threshold, the government implements school closure and movement restriction measures (MoH A/373 Order. 2022). According to the previous years' experience, the Mongolian government implemented school closure and movement restrictions once during an influenza and ILI peak.

The Mongolian health insurance scheme is based on the Diagnostic Related Groups (DRG) model and payments were prospectively sent to the ILI healthcare providers. International Code of Diseases-10 (ICD-10) J00-J22 are and those who met ILI and SARI case definitions paid for the standard medication and treatment from the National Health Insurance (NHI), if additional services are needed individuals must pay from out-of-pocket.

Based on the extant literature, the highest economic burden is estimated to be on working adults. However, the evidence of the OOP and economic burden of ILI among risk groups (children below 5 years old, pregnant women, and older adults) is not clearly defined. We aim to determine the economic burden among those populations.

Purpose

This study aims to assess the economic burden of ILI or SARI from a societal perspective in Mongolia.

1. To estimate the cost per episode by ILI and SARI visits.
2. To assess the economic burden of ILI and SARI among the study population.
3. To assess the annual economic burden of ILI/SARI cases detected in sentinel sites.

II. LITERATURE REVIEW

Burden of Disease

Seasonal influenza has an enormous socioeconomic impact and causes significant morbidity and mortality worldwide. Globally, approximately 1 billion people get infected with influenza resulting in 3–5 million hospitalizations and 290,000–650,000 deaths annually (WHO, 2022). In northern hemisphere countries, seasonality usually occurs during winter, mainly during the cold season. In tropical countries, seasonality is unclear and outbreaks occur throughout the year, specifically during the rainy season (Cox, 2014).

Seasonal influenza A, B, and other respiratory pathogens such as Respiratory Syncytial Virus (RSV), adenovirus, rhinovirus, and seasonal coronavirus are the main causes of outbreaks. Despite the cold weather, seasonality in Mongolia often starts with the RSV outbreak increasing pediatric hospital demand.

Based on current studies, seasonal influenza and ILI significantly impacted both households and the government. ILI and SARI cases accounted for a large portion of illness and productivity losses. There is evidence of the significant yearly socio-economic burden associated with ILIs and SARIs, especially for those who are in the high-risk group. The burden among older people, children, pregnant women, and people with chronic diseases was higher than the general population.

Methods to estimate BoD

The impact of disease on health occurs in two ways: directly (as a disease) and indirectly (affecting individuals' well-being and productivity). Disease burden estimates can provide a comprehensive and comparable assessment of death and severe disease. Therefore, health research investments and national preventive measures can be planned effectively with these estimates. The WHO Manual for Estimating Diseases Burden Associated with Seasonal Influenza is the most commonly used method to estimate the burden of seasonal influenza and ILI (World Health Organization, 2015).

Before proceeding to the estimation, relevant data should be reviewed for quality, relevance, completeness, and representativeness. The first step for estimating the disease burden is to have an accurate numerator, for example, the total ILI/SARI visit or admission number. Where the data on the denominator population is available, the best measure of disease burden in the population is the annual incidence of influenza-associated SARI by age and gender. However, these data should be adjusted using respective age groups or gender population data. Other epidemiological or laboratory variables and specific risk groups data can be used for estimation. Results of these estimates are often presented as ILI/SARI incidence among risk groups, maximum attack rate, hospitalization, intensive care unit admission, or death.

Disease incidence of influenza-associated ILI is captured only in terms of morbidity, which is defined as "an episode of illness or disease associated with influenza." If the appropriate data are available, the incidence rate can be estimated from ILI sentinel sites that record information from patients who seek ambulatory care. As the number of clinically-diagnosed ILI cases is likely to be large, not all ILI cases may be confirmed with valid laboratory tests. The percentage of clinically confirmed and laboratory-tested ILI cases is therefore extrapolated to estimate the total number of influenza-associated ILI cases. The incidence rate is calculated by dividing the total number of influenza-associated ILI cases by the estimated catchment population of the sentinel site.

Cost of Illness

The cost-of-illness (COI) studies convert the burdens associated with certain illnesses into economic and monetary values to measure the socioeconomic costs that are inevitably incurred by a given society in association with certain illnesses. The estimated costs provided by COI studies provide an important basis for estimating the amounts of public health resources spent and productivity losses incurred and thereby make it possible to quantify the socioeconomic burdens that illnesses impose on society in general. These estimates are crucial to policymakers' decision making.

COI studies can be divided into two categories: incidence-based or prevalence-based. The incidence-based approach involves estimating the socio-economic cost of a given illness from the initial stage to the patient's complete recovery or death. This involves estimating not only the economic burden imposed by the illness but also the cost of future health-related losses, including those caused by sequela. This approach allows the researcher to identify economic losses over time, from the present into the future, but makes it impossible to considers patients who have already suffered from the same disease.

Contrary to the incidence-based approach, the prevalence-based approach considers economic burdens accruing not only for existing patients suffering from a given illness for a fixed period of time but also for future and potential patients. This approach is well suited to estimating the economic costs of an illness at certain points in time but may not allow the researcher to estimate the cost accrued throughout the lifespan of the illness, from its initial stage to the patient's complete recovery (or death). Furthermore, this approach may not be amenable to estimating the costs of frequent yet short-lived illnesses that do not last long enough for the researcher to find and identify suitable patients within a given period.

Therefore, based on how data are collected, COI can be categorized into a top-down or bottom-up approach. A top-down approach uses national level data and then separates the diseases one by one to estimate individual cost. Conversely, the bottom-up approach uses all relevant individual illnesses and then estimates the total socioeconomic cost at the national level. While this method is more accurate than the top-down approach, it is challenging to estimate without complex individual data.

Economic Burden of a Disease

Estimates of economic burden capture the economic impact of a disease or illness of interest on both the health and non-health sectors at both microeconomic and macroeconomic levels. Economic burden is defined by cost-of-illness studies that estimate direct and indirect costs owing to disease and injury.

Generally, the human capital and willingness-to-pay approach is used to estimate indirect socioeconomic costs of illness. The human capital approach is commonly used by researchers and this approach estimates the current value of human life as the discounted future expected outcome. In other words, this approach focuses on the opportunity costs of illness and death. Results of these estimates are presented as losses of future income due to the illness.

The willingness to pay approach estimates the economic value of something that cannot be easily converted into a monetary sum by asking how much they are willing to pay for it. Thus, people value monetary sums as they see fit, and results often vary. In some studies, researchers used closed-ended questions for better classification.

Perspectives of analysis

Before delving into the study, the perspective of analysis should be determined. The three main perspectives include patient, societal, and payer. The payer perspective focuses on the costs of illnesses that are paid by insurers and not patients. The patient perspective requires the researcher to analyze and estimate the costs paid by patients owing to given illnesses. These costs include direct healthcare and non-healthcare costs and indirect costs. The direct healthcare costs include the copayments made by patients, the non-covered costs, and the costs of informal medical services, while the direct non-healthcare costs include the expenses patients have to pay to receive medical services, such as transportation expenses.

The societal perspective leads to the estimation of the costs estimated from both the payer and patient perspectives and the losses of societal productivity caused by the given diseases. In other words, the costs estimated based on this perspective include the costs of lost labor and productivity due to patients taking leaves of absence or dying prematurely. These costs may also encompass the costs of declines in quality of life and the psychological suffering of patients.

Components of costs

Existing literature generally analyzed direct costs, indirect costs, and intangible costs. Direct cost is how much money is spent to cure or manage illness or the amounts of money spent at the health facilities for the treatment. It is further divided into medical costs and non-medical costs. The direct medical costs include the cost of outpatient/inpatient service, medication, and laboratory tests. However, direct non-medical costs include service charges for transportation, food, bed stays, or caregiving.

The indirect costs are mainly productivity losses, which are estimated by using hospitalization days as the number of lost working days and the amount of time spent in outpatient visits as losses of working time. Moreover, the intangible costs represent a decline in quality of life and psychological suffering of patients and their loved ones. These costs are very difficult to define and quantify with precision.

Sample population

Seasonal influenza vaccination is one of the best measures to minimize morbidity and mortality. In 2012, the WHO vaccine position paper outlined healthcare workers, older adults, pregnant women, and individuals with underlying health conditions and children as a priority group for vaccination owing to potential increased risk of severe disease. Following this vaccination policy, Member States adapted their local seasonal influenza vaccination policy. According to this policy, Mongolia convened NITAG to select priority groups for seasonal influenza and the National Center for Communicable Diseases, the National Influenza Center provided relevant pieces of evidence such as seasonal influenza BoD, which highlighted the highest burden among children below 5 years (Darmaa et al., 2021). A Decision was made to prioritize healthcare workers, pregnant women, children, and the older population. We selected THREE of these risk groups to estimate the economic burden of seasonal influenza and ILI.

WHO Manual for estimating the economic burden of seasonal influenza

A study of the economic burden of influenza can inform the decisions of policy-makers to introduce the influenza vaccine by providing an estimate of the overall magnitude of the economic costs of the influenza disease in a given country. Approaches to economic burden analysis can vary from study to study. To help standardize the approaches for the economic burden of influenza, the WHO developed a standard protocol. A proposed calculation of the total economic burden was presented as "Direct medical cost + Direct non-medical cost + Indirect cost." The manual provides detailed instructions for estimating the economic burden of seasonal influenza. Furthermore, it offers prospective or retrospective study data collection based on the existing data.

The manual provides guidance on the estimation of outpatient and inpatient visit costs, and indirect costs (productivity costs). Outputs of this manual provide cost per inpatient episode, cost per outpatient episode, OOP per inpatient and outpatient episode, and total treatment cost per patient, with and without indirect costs. Generic questionnaires are included in the appendices and countries are adapting it to estimate the economic burden of seasonal influenza.

Table 1. Table of Evidence part 1.

Author/ Date	Methodology/Design	Purpose	Results
LaiLeng Woo, et al. 2019(Woo et al., 2019)	Systematic review / The economic burden of disease	Assess cost studies of chronic obstructive pulmonary disease and analyze cross-country cost comparisons in Asia-Pacific.	Annual total societal costs of COPD ranged from $4398 to $23049 per capita in Japan and $453 to $12167 in South Korea. There were no intracountry comparison estimates for the remaining countries.
Evgeniya N Antonova, et al. 2012(Antonova et al., 2012)	Systematic review/ Burden of disease, and economic burden	To summarize the influenza burden (in terms of health outcomes and economic burden) in children in Western Europe via a systematic literature review.	Young children and those with severe illness had the highest rates of health care use. Influenza in children also led to absenteeism from day care, school, or work for the children, their siblings, and their parents. The average (mean or median) length of absence from school or day care associated with confirmed influenza ranged from 2.8 to 12.0 days for the children, from 1.3 to 6.0 days for their siblings, and from 1.3 to 6.3 days for their parents.
Tais F. Galvao, et al. 2013(Galvao et al., 2013)	Systematic review / Vaccine effectiveness	To assess the effects of the inactivated influenza virus vaccine on influenza outcomes in pregnant women and their infants.	Influenza vaccination in pregnant women significantly reduced the incidence of influenza-like illness (ILI) in mothers and their infants when compared with control groups (high-quality evidence) and reduced the incidence of laboratory-confirmed influenza in infants (moderate-quality evidence). No difference was found with regard to ILI with fever higher than 38∘C (moderate-quality evidence) or upper respiratory infection (very-low-quality evidence) in mothers and infants.
Trung Quang Vo, et al 2017(Quang Vo et al., 2017)	Social and economic burden of illness	To estimate the cost of illness based on a social perspective of ILI cases.	The average cost of treatment associated with ILI was US$ 88.09 per case for all age groups; direct non-medical cost was higher compared to direct medical cost: 39.5% in pharmacies, 71.1% in clinics, and 64.2% in hospitals. The indirect cost was US$27.49 per episode.

Lei Zhou, et al. 2013(Zhou et al., 2013)	Cost of illness of influenza related hospitalizations among Severe Acute Respiratory Infections (SARIs)	To better understand the economic burden of influenza-related hospitalizations among patients among China in different age and risk categories.	A total of 106 laboratory-confirmed influenza-related hospitalizations were identified, 60% of which were children. The mean (range) direct medical cost was $1,797 ($80–$27,545) for all hospitalizations, and the median (IQR) direct medical cost was $231 ($164), $854 ($890), and $2,263 ($7,803) for children, adults, and older adults, respectively. Therapeutics and diagnostics were the two largest components of direct medical cost, comprising 57% and 23%, respectively.
Chisato Imai, et al. 2018(Imai et al., 2018)	Systematic review / Direct epidemiological and economic effects of seasonal influenza vaccination.	To synthesize the latest evidence of the direct epidemiological and economic effectiveness of seasonal influenza vaccination among HCW.	While the overall incidence of absenteeism was not changed by vaccine, ILI absenteeism was significantly reduced. The duration of absenteeism was also shortened by vaccination.
Ru-ning Guo, et al. 2016(Guo et al., 2016)	Time series Poisson Generalized Additive Model	The impact of influenza on outpatient visits, hospital admissions, and deaths have not been fully demonstrated to date in south China.	We determined that 10.7% of outpatient visits were associated with ILI and 1.88% were associated with influenza. ILI also had a significant influence on the hospitalization rates ($P < 0.05$), but mainly in populations <25 years of age.
Xiaozhen Lai, et al. 2021(Lai et al., 2021)	Economic burden of Influenza like illness	To examine the prevalence of ILI, we identified healthcare-seeking behaviors, economic impact of ILI, and its influencing factors among three priority groups during the 2018–19 influenza season.	The average economic burden was CNY 1647 (USD 237.2) for children, CNY 951 (USD 136.9) for chronic disease patients, and CNY 1796 (USD 258.6) for older adults. A two-part regression showed that age, gender, whether the only child in the family, region, and household income were important predictors of ILI economic burden among children, while age, region, place of residence, basic health insurance, and household income were significant predictors of ILI economic burden among chronic disease patients and older adults.

Magali Lemaitre, et al. 2022(Lemaitre et al., 2022)	Economic burden of disease	Estimating the epidemiological and economic burden of severe influenza in France during eight consecutive influenza seasons (2010–2018).	The average number of respiratory hospitalizations indirectly related with influenza (i.e., influenza associated) was 31,490 (95% confidence interval [CI]: 24,542–39,012), with an average cost of €141 million (range: 54–217); 70% of these hospitalizations and 77% of their costs concerned individuals ≥65 years of age (65+). More than 90% of excess mortality was found in 65+ subjects.
Sierk D. Marbus, et al. 2020(Marbus et al., 2020)	Cost of disease	To estimate the incidence of hospitalization for influenza virus infection and associated hospitalization costs in adult patients in the Netherlands during two consecutive influenza seasons.	The arithmetic mean hospitalization cost per influenza patient was €6128 (95% CI €4934–€7737) per patient in 2014–2015 and €8280 (95% CI €6254–€10,665) in 2015–2016, potentially reaching total hospitalization costs of €28 million in 2014–2015 and €20 million in 2015–2016. Influenza virus infections lead to 1.8–3.5 hospitalized patients per 10,000 persons, with mean hospitalization costs of €6100–€8300 per adult patient, resulting in 20–28 million euros annually in The Netherlands.
Gatien de Broucker, et al. 2020(de Broucker et al., 2020)	Systematic review / Cost of nine pediatric infectious illness	To gather cost data and relevant parameters for hepatitis B, pneumonia, meningitis, encephalitis caused by Japanese encephalitis, rubella, yellow fever, measles, influenza, and acute gastroenteritis in children in low- and middle-income countries.	No cost-of-illness studies with cost estimates for hepatitis B, measles, rubella, or yellow fever from primary data. Most estimates were from countries in Gavi preparatory (28%) and accelerated (28%) transition, followed by those who initiated self-financing (22%) and those not eligible for Gavi support (19%). Thirteen articles compared household expenses to manage illnesses with income and two articles with other household expenses, such as food, clothing, and rent. An episode of illness represented 1–75% of the household's monthly income or 10–83% of its monthly expenses.
Tanja Fensm et al. 2021(Fens et al., 2021)	Systematic review	To identify economic evaluations of seasonal influenza vaccines that considered AEFIs.	Most studies used the societal perspective (64%) and evaluated vaccination of children (37%). Where considered, studies included direct medical costs of AEFIs (90%), indirect costs (27%), and disutilities/quality-adjusted life years loss due to AEFIs (37%).

Gyeongseon Shin, et al. 2022(Shin et al., 2022)	Cost effectiveness	To investigate the cost-effectiveness of expanding the universal vaccine fund to include those aged 50–64.	From a societal perspective, the proposed policy would reduce costs by USD 68 million. From a healthcare perspective, the cost is USD 4318 per quality-adjusted life years.
Kristin L. Nichol, et al. 2008(Nichol et al., 2009)	Prospective cohort study / Burden of illness, and vaccine effectiveness	To clarify the burden of ILI and the benefits of vaccination among adults aged 50–64 years old.	In the multivariable regression analyses, vaccination was associated with a significant reduction in the rate of ILI (adjusted odds ratio, 0.48; 95% confidence interval, 0.27–0.86) and fewer days of illness, absenteeism, and impaired on-the-job performance.
M. N. Niang, et al. 2018(Niang et al., 2018)	Sentinel surveillance data / Burden of Disease	To estimate the burden of flu-association ILI visits on total clinic outpatient visits during three consecutive annual influenza seasons in Senegal, 2013–2015.	The estimated proportional contribution of influenza-associated ILI was, per 100 outpatients, 1.2 (95% CI 1.1–1.3), 0.32 (95% CI 0.28–0.35), 1.11 (95% CI 1.05–1.16) during 2013, 2014, 2015, respectively. The age-specific outpatient visits proportions of influenza-associated ILI were higher among children under 5 years (0.68%, 95% CI: 0.62–0.70). The predominant virus during years 2013 and 2015 was influenza B while A/H3N2 subtype was predominant in 2014.
Giedre Gefenaite, et al 2018(Gefenaite et al., 2018)	Sentinel surveillance data / Burden of Disease	To estimate the incidence of medically attended influenza-associated ILI and hospitalizations due to SARI presenting to public healthcare facilities.	The highest ILI and influenza incidence was among children aged 0–4 years. Up to 0.3% of the Romanian population were annually reported with ILI, and 0.01% was hospitalized with SARI, of which as much as one-third could be explained by influenza.

Kiyosu Taniguchi, et al 2020(Taniguchi et al., 2021)	Systematic review / Vaccine effectiveness meta-analysis	To synthesize existing evidence on the epidemiology, vaccine effectiveness (VE), and economic burden of seasonal influenza in older adult population.	The maximum reported attack rate was 55.2% and in the 16 articles reporting mortality rates, case fatality rates varied from 0.009% to 14.3%. Most hospitalizations were in people aged >60; healthcare costs were partially mitigated by vaccine administration. Meta-analysis estimated overall VE of 19.1% (95% CI: 2.3% - 33.0%) with a high proportion of heterogeneity (I2: 89.1%). There was a trend of lower VE in older people (40.1% [−57.3-77.2] in the <65 group; 12.9% [−8.0-29.8] in those 65; *P* = .21).
Irene Giacchetta, et al 2021(Giacchetta et al., 2022)	Systematic review / Burden of disease	To provide a comprehensive summary of the available evidence on the burden of seasonal influenza in Italy.	The synthesis of results showed that patients with chronic conditions have an increased risk for complications up to almost three times as compared to healthy people. Hospitalizations due to influenza can occur in as much as 5% of infected people depending on the study setting. Excess death rates were over sixfold higher among older adults compared to the rest of population.
Y. Tsai, et al 2014(Tsai et al., 2014)	Burden of Disease	To assess work absenteeism due to ILIs.	The mean number of work hours lost per ILI episode was 23.6 in 2007–8 and 23.9 in 2008–2009. The proportion of employees with at least one ILI was 1.7% in 2007–8 and 1.2% in 2008–9. In both seasons, the proportion with ILI was higher among older (2.1 and 1.5%) and hourly workers (2.0 and 1.3%), workers in the southern region (1.9 and 1.3%) and those in oil, gas, or mining industries (1.9 and 1.4%).

W. John Paget, et al 2010(and all EPIA collaborators et al., 2010)	Sentinel surveillance data / Burden of Disease	To provide the necessary information to make evidence-based decisions regarding influenza immunization recommendations for children.	ILI consultation incidence during 2002/2003–2008 revealed that influenza infections that presented for medical attention as ILI affected between 0.3% and 9.8% of children aged 0– 4 and 5–14 years in England, Italy, The Netherlands, and Spain in an average season. With the exception of Spain, these rates were always higher among children aged 0–4 years. Across the six seasons analyzed (five seasons were analyzed from the Italian data), the model attributed 47– 83% of the ILI burden in primary care to influenza virus infection in the various countries, with the A(H3N2) virus playing the most important role, followed by influenza viruses B and A(H1N1).
Musse Tadesse, et al 2020(Tadesse et al., 2020)	Sentinel surveillance data / Burden of Disease	To address the information gap by estimating the burden and seasonality of medically attended influenza like illness in Ethiopia.	The Incidence rate of ILI was higher in the age group of 15–44 years of age [‘Incidence rate (R) = 254.6 per 100,000 population’, 95% CI; 173.65, 335.55] and 5–14 years of age [R = 49.5, CI 95%; 31.47, 130.43]. The seasonality of influenza has two peak seasons: between October and December and from April to June.
Josephine Mauskopf, et al 2013(Mauskopf et al., 2013)	Systematic review / Burden of disease	To review the published literature on seasonal influenza to assess the differences between complications and mortality rates for those adults at high risk of influenza complications.	Rates of hospitalization and pneumonia or lower respiratory tract infection for those with chronic conditions or those who are immunocompromised are substantially higher than those in people over age 65 but without additional high-risk factors. A person who is hospitalized and has a laboratory-confirmed influenza diagnosis has a probability of intensive care unit admission of between 11.8–28.6% and death of between 2.9–14.3%.

Table 2. Table of Evidence part 2.

Author/ Date	Conclusion	Implication for Future research
LaiLeng Woo, et al. 2019	Results of this review showed high-cost variations between countries.	We propose that researchers conducting burden-of-illness studies use standard methods and reporting formats to support cross-country comparisons.
Evgeniya N Antonova, et al. 2012	The influenza burden among children is substantial and has a significant direct impact on the ill children and an indirect impact on their siblings and parents.	The identified evidence regarding the burden of influenza may help inform both influenza antiviral use in children and pediatric immunization policies in European countries.
Tais F. Galvao, et al. 2013	Maternal vaccination against influenza was shown to prevent ILI in women and infants; no differences were found for other outcomes.	As the quality of evidence was not high overall, further research is needed to increase confidence and could possibly change these estimates.
Trung Quang Vo, et al 2017	The cost of illness of ILI was, therefore, the reason for the economic burden of influenza patients and their families.	This study provides a database for future research and programs, and policies that can be adopted for influenza or ILI in Vietnam.
Lei Zhou, et al. 2013	Direct medical cost of influenza-related hospitalizations imposes a heavy burden on patients and their families in China.	To increase vaccination rate and develop targeted national preventive strategy.
Chisato Imai, et al. 2018	All published economic evaluations consistently found that the immunization of HCW was cost saving based on crude estimates of avoided absenteeism by vaccination	A better understanding of the incidence of absenteeism and comprehensive economic program evaluations are required to ensure the best possible management of ill HCWs and the investment in HCW immunization in increasingly constrained financial environments.
Runing Guo, et al. 2016	ILI is a feasible indicator of influenza activity. Both ILI and influenza have a large impact on outpatient visits.	The impact of influenza on the mortality rate requires further evaluation.

Xiaozhen Lai, et al. 2021	A large economic burden of ILI was highlighted, especially among older adults with less income and larger medical burdens, as well as children, with higher prevalence and higher self-payment ratios.	It is important to adopt targeted interventions for high-risk groups, and this study can help national-level decision-making on the introduction of influenza vaccination as a public health project.
Magali Lemaitre, et al. 2022	The present study highlighted the major public health burden of influenza and its severe complications, especially in 65+ subjects.	Further studies should assess the organizational impact of influenza epidemics (overwork in hospital departments, increased sick leave in the general population, ...), which is an important aspect that was not evaluated in the present study.
Sierk D. Marbus, et al. 2020	The highest arithmetic mean hospitalization costs per patient were found in the 45–64-year age group.	These influenza burden estimates could be used for future influenza cost-effectiveness and impact studies.
Gatien de Broucker, et al. 2020	Articles that presented both household and government perspectives showed that most often, governments incurred greater costs than households, including non-medical and indirect costs, across countries of all income statuses, with a few notable exceptions.	Additional information on whether common situations preventing the application of official clinical guidelines (such as medication stock-outs) occurred would help reveal deficiencies in the health system. Improving the availability of cost-of-illness evidence can inform the public policy agenda about healthcare priorities and can help to operationalize the healthcare budget in local health systems to respond adequately to the burden of illness in the community.
Tanja Fensm et al. 2021	The overall impact of AEFIs on the cost-effectiveness outcomes was found to be low.	We urge their inclusion in economic evaluations of seasonal influenza vaccines to reflect comprehensive reports for the decision makers and end-users of the vaccination strategies.
Gyeongseon Shin, et al. 2022	The influenza vaccine for adults aged 50–64 appears to be cost-saving or cost-effective and, thus, should be considered for the NIP.	Further research is necessary to determine the social contact as well as disease and vaccination characteristics.
Kristin L. Nichol, et al. 2008	ILIs were common among our study participants, accounting for a large portion of illness, work loss, and impaired work performance during the influenza season. Vaccination was associated with substantial health and productivity benefits.	Vaccine delivery should be improved for this high-priority group.

M. N. Niang, et al. 2018	Influenza viruses cause a substantial burden of outpatient visits particularly among children under 5 years.	Highlight the need of vaccination in risk groups.
Giedre Gefenaite, et al 2018	During each influenza season, a substantial number of persons in Romania suffer from influenza-related ILI or are hospitalized owing to influenza- associated SARI.	To improve vaccination uptake and increase awareness of influenza prevention and treatment.
Kiyosu Taniguchi, et al 2020	Despite differences between studies that make comparisons being challenging, the influenza burden in older Japanese adults is significant. While vaccines are effective, current vaccination programs offer suboptimal protection.	Health economic data and cost-effectiveness analyses were limited and represent areas for policy- relevant future research.
Irene Giacchetta, et al 2021	There is evidence of the significant burden that influenza places each year, especially on high-risk groups.	These data should be used to inform public health decision-making.
Y. Tsai, et al 2014	Our results indicate that the disease burden associated with ILIs in the working population is not trivial.	Deserves attention from policymakers and health care professionals to design effective strategies to reduce this burden.
W. John Paget, et al 2010	Influenza virus infections explained the majority of pediatric ILI consultations in all countries.	The next step will be to apply the EPIA modelling approach to severe outcomes indicators (i.e., hospitalizations and mortality data) to generate a complete range of mild and severe influenza burden estimates needed for decision making concerning pediatric influenza vaccination.
Musse Tadesse, et al 2020	Significant morbidity of influenza like illness was observed with two peak seasons of the year and seasonal influenza A (H3N2) remains the predominantly circulating influenza subtype.	Further studies need to be considered to identify potential risks and improving the surveillance system to continue early detection and monitoring of circulating influenza virus in the country has paramount importance.
Josephine Mauskopf, et al 2013	The key finding was that those over 65 years of age but without additional high-risk factors had a low risk of influenza complications.	Information about influenza complication rates and resource use, including influenza vaccines, chemoprophylaxis and treatment strategies for different high-risk groups, is needed to evaluate new interventions.

III. METHODS

Survey Design

This is a cost-of-illness study presenting findings as per episode. Overall, the *WHO Manual for Estimating the Economic Burden of Seasonal Influenza (v4)* was used to adapt questionnaires, analyze data, and present data. Societal perspective costs were calculated according to WHO methods.

Table 3. Overview of types of data collected and tools/resources used.

Types of data to be collected	Tools or resources
Outpatient, inpatient costs	Patient survey, follow up survey
Productivity losses for patients and caregivers	Out-of-pocket cost survey

Target Populations

The age-specific population size was obtained from the National Bureau of Statistics in Mongolia and stratified by area (urban/rural) using the proportion of people living in urban areas. Furthermore, three of the SAGE recommended risk groups are included in this study: children from 6 months to 5 years; pregnant women in their second and third trimesters; older people (above 65 years of age).

Inclusion Criteria

- Agreed to participate.
- Met with case definition

Exclusion Criteria

- Prevented from participating by subject or their guardian.

Case Definition

The WHO global influenza surveillance standards defined surveillance case definitions are used.

Influenza-Like-Illness (ILI) case definition:

- Measured fever of ≥ 38 C°
- Cough;
- With onset within the last 10 days.

Severe Acute Respiratory Infection (SARI) case definition:

- History of fever or measured fever of ≥ 38 C°;
- Cough;
- With onset within the last 10 days;
- Requires hospitalization.

Sample size and calculation

Children from 6 months to 5 years old were 426,451 (rural = 222,969; urban = 203,482) and there was a total of 135,707 (rural = 72,760; urban = 62,947) older people. Pregnant women in their second and third trimester were 39,790 (rural = 22,042; urban = 17,748) nationwide, according to the National Bureau of Statistics (NBS). We collected data throughout the influenza season (October to May). Respondents who agreed to participate were questioned regarding direct and indirect costs associated with ILI. We randomly selected 10 provinces and 8 districts hospitals as the data collection sites. The estimated number of participants were based on previous influenza season data by each group using the Krejcie and Morgan sample size calculation.

$$s = X^2NP(1-P) \div d^2(N-1) + X^2P(1-P).$$

s = required sample size.

X2 = the table value of chi-square for 1 degree of freedom at the desired confidence level (3.841).

N = the population size.
P = the population proportion (assumed to be .50 since this would provide the maximum sample size).
d = the degree of accuracy expressed as a proportion (.05).

Table 4. Targeted sample size for study groups.

Sample size	**6 months to 5 years**		**Pregnant women**		**65 and above**	
	Out	*In*	*Out*	*In*	*Out*	*In*
UB	300	300	300	100	300	100
Province	300	300	300	100	300	100
Total	**1200**		**800**		**800**	

* *Out* = *Outpatient*; In = Inpatient; UB = Ulaanbaatar

Geographical classification

Mongolia is divided into four regions based on their environmental status. It includes Western (Bayan-Ulgii, Khovd, Uvs, Zavkhan, Gobi-Altai), Khangai (Bayankhongor, Uvurkhangai, Arkhangai, Bulgan, Khovsgol), Central (Umnugobi, Dornogobi, Dundgobi, Tuv, Selenge), and Eastern (Khentii, Sukhbaatar, Dornod) regions. While the highest point of the western region (Altain Nuruu) is 4,300-meters , the Khangai region has a 3,500-meter height (Khangain nuruu). However, the Central and Eastern regions have 900 and 1500-meter heights. Regarding climate conditions, the northern part of the country is colder and windy with forests. However, the southern part of the country is drier and warmer, and covered in a desert land.

Figure 1. Geographic classification of Mongolia

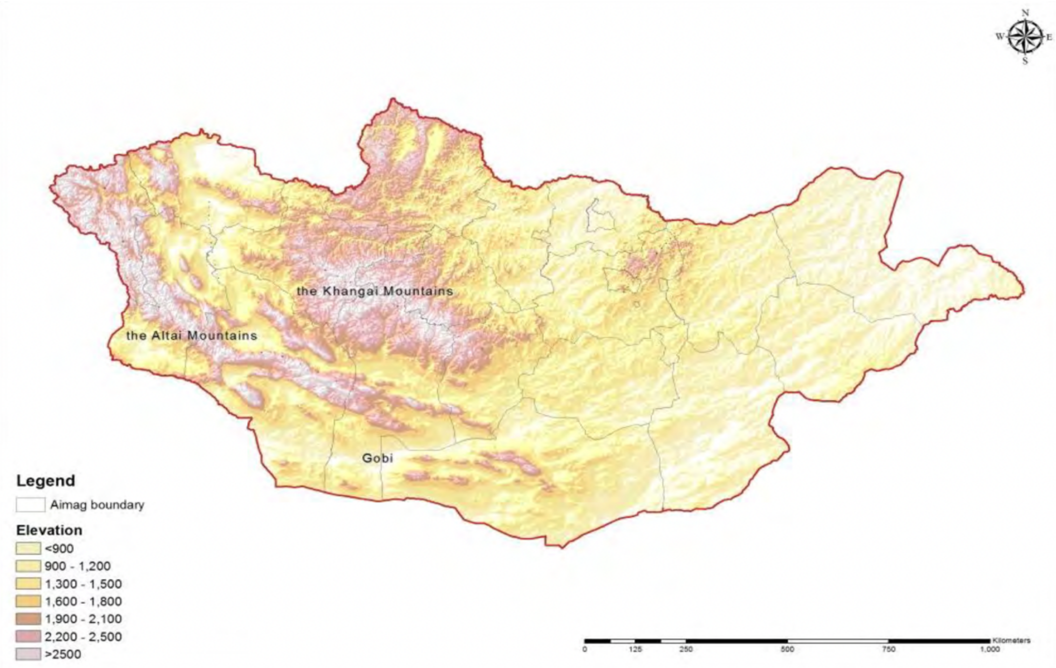
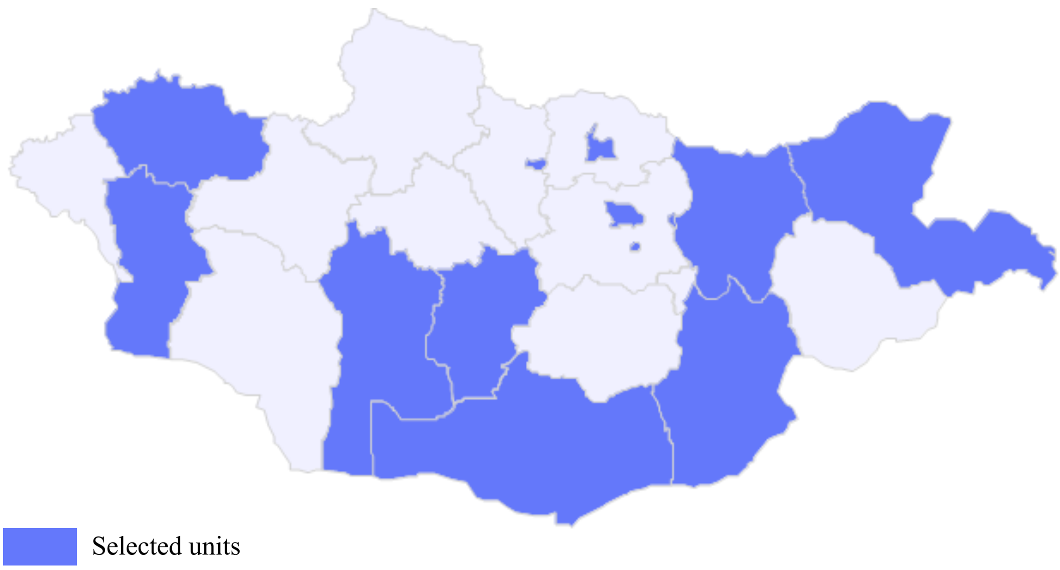


Table 5: List of participating health facilities

District	Province	Tertiary
Baganuur	Bayankhongor	1st Maternity
Bayangol	Darkhan-Uul	2nd Maternity
Bayanzurkh	Dornod	3rd Maternity
Chingeltei	Dornogobi	National Center for
Khan-uul	Khentii	Maternal and Child
Nalaikh	Khovd	Health
Songinokhairhan	Orkhon	
Sukhbaatar	Umnugobi	
	Uvs	
	Uvurkhangai	

Figure 2. Map of participating health facilities



Measures of resources and costs

Costs included

Direct medical costs (paid by government, health facility, patient, or other sources). Direct cost is defined as all costs resulting from resource use that are completely attributable to the use of a health care intervention or illness. The direct cost will be divided into medical costs (physician charges, drugs, diagnostic expenditures, and bed rent, other hospital charges, and informal payments) and direct non-medical costs (travel, food, and material purchased like blankets, mosquito bed nets, etc.).

1. Diagnostic and monitoring tests.

2. Inpatient and outpatient visits to relevant departments and wards in which the surveillance component is implemented (e.g., medicine, surgery, pediatric, emergency, and intensive care).
3. Prescribed drugs and therapies for influenza and related complications.

Direct non-medical costs (paid by patient or caregiver)

1. Transport to and from health facility.
2. Food and lodging for patient and caregiver while seeking care.
3. Child care while seeking care.
4. Other out of pocket expenses related to seeking care.

Indirect costs of productivity losses for patient:

The term indirect costs are the expenses incurred from the missing or reducing of work productivity as a result of the morbidity and mortality associated with a given disease. Indirect costs typically consist of work loss, worker replacement, and reduced productivity from illness and disease.

1. Short term days of work missed owing to illness during influenza episodes.
2. Long term days of work expected to be missed owing to sequelae.
3. Long term days of work missed owing to death.

Indirect costs of productivity losses for caregiver:

1. Short term days of work missed owing to providing care for influenza patient.

Costs excluded

1. Costs of MRI and CT scan.
2. Costs of non-influenza-related drugs and therapies (e.g., anti-malarial medications).
3. Costs of diagnosis and treatment of co-morbidities and chronic conditions not directly related to influenza;

4. Intangible costs related to pain and suffering.
5. Evaluation-specific costs; and
6. Value of project team staff time for project management, technical assistance, and evaluation.

Data collection and information sources

Primary data were collected from the patient via an interview and the hospital database. After obtaining written consent or assent *(Annex 1)*, project staff interviewed each patient and their caregiver using survey questionnaires *(Annex 2; Annex 3; Annex 4)*. Nasopharyngeal or oropharyngeal swabs were collected from patients who met case definitions of ILI and SARI. Sample collection, transportation, and analysis followed the protocol approved by the Minister of Health, Mongolia. Samples were tested for seasonal influenza and ILI virus by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) using primers and all outcomes were measured at the individual level.

Data Management & Analysis

Survey response data, including unique ID, were entered using a standard data entry interface Epi Info by trained personnel. Participant names were not entered into the database. Data were cleaned and corrected using original survey documents by a data manager. To maintain the confidentiality of responses, data were stored on a device with secure login and weekly off-site backup, and hard copies were securely stored in a central location in-country for three years.

The cost analysis will be conducted using a bottom-up approach (bottom-individual; up-societal costs). Average costs will be calculated for each particular type of cost. The costs consist of direct medical, direct non-medical, and indirect costs. A human capital method will be used to determine the cost of absenteeism from paid employment. This measure considers the social value of an individual to equal future potential production, measured by the value of anticipated lifetime income. A limitation of this method is that it does not consider unemployment (retired people or those with disability), although this was corrected by assigning a value equal to the minimum wage or average salary of their profession. Costs were collected in Mongolian Tugrik (₮) and converted to US dollars (USD) based on the data collection period conversion rate.

Outcomes, costs, and use of resources were reported as the median with interquartile and mean values with standard deviations for each scenario. Mean differences between scenarios in cost, outcomes, and resources, and 95% confidence intervals were calculated. If cost data do not confirm to the assumptions for the standard statistical test, the non-parametric will be performed.

To address potential biases owing to an incomplete follow-up, data interviews were conducted to fill missing values. There is potential BIAS due to non-response at each follow-up. The significance level of the model was set at 5%. The STATA MP 14 for MAC OSX and MS Excel were used for statistical analysis.

Annual ILI and SARI economic burden

The annual economic burden of ILI and SARI were calculated as mean per episode costs for outpatient and inpatient visits. The Mean and Confidence Intervals for mean per episode were multiplied as the number of reported ILI/SARI cases at the seasonal influenza sentinel surveillance sites between 2021 and 2022. The data were extracted from the National Influenza Center of the National Center for Communicable Diseases.

IV. RESULTS

General characteristics of the study groups

A total of 2779 participants agreed to participate in study. Amongst participants, 1227 (44.2%) were children below 5 years old, 778 (28.0%) were people above 65 years, and 774 (27.9%) were pregnant women. Furthermore, 1044 (38.1%) participants were hospitalized owing to SARI and 1703 (61.9%) went to outpatient health centers seeking health care.

Table 6. Number of participants by study groups and admission.

Study groups	Outpatient		Inpatient		Total
Province	n	%	n	%	
Children <5 years	323	52.44	293	47.56	616
65 and above	303	76.13	95	23.87	398
Pregnant women	285	64.48	157	35.52	442
Capital					
Children <5 years	267	44.43	334	55.57	601
65 and above	241	66.03	124	33.97	365
Pregnant women	284	87.38	41	12.62	325

Overall, one of three (29.63%) participants went to other health service providers before coming to the health facilities designated as the study site. Among the study participants, children below 5 years old who had the highest rate (36.84%) went to the health service provider.

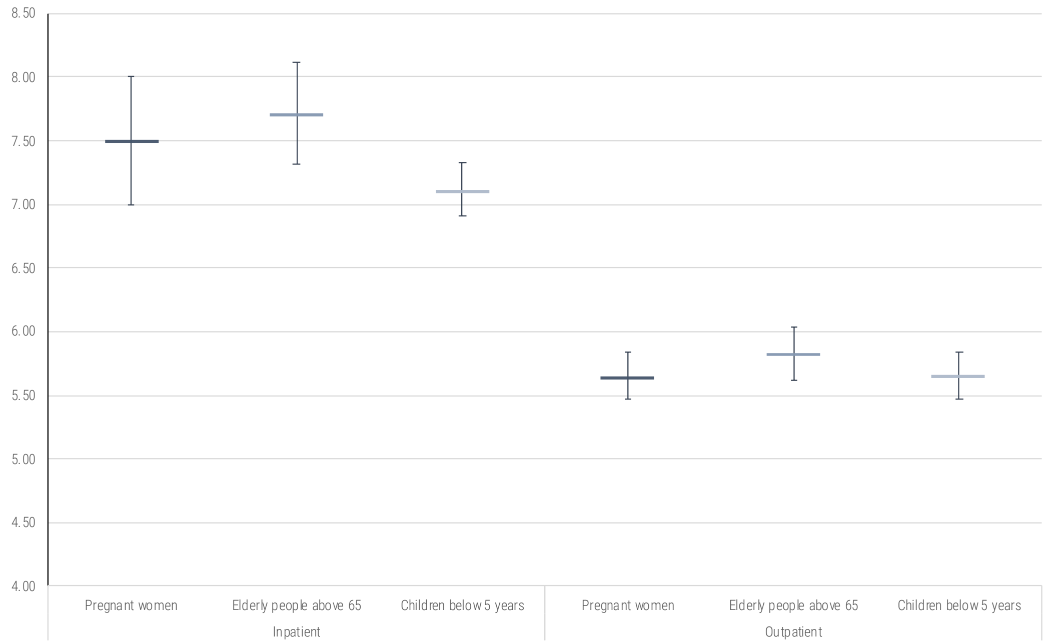
Table 7. Representation of visits to a health service provider before coming to study health facility

Study group	Yes		No	
	n	%	n	%
Children below 5 years	399	36.84	684	63.16
Older people above 65	182	26.76	498	73.89

Pregnant women	145	21.11	542	78.89
Total	726	29.63	1724	70.37

The average length of stay was 5.58 (CI 5.46 – 5.69) among outpatients and 7.27 (CI 7.10 – 7.45) of inpatient admission. Among the target groups, older people above 65 years had stayed longer than the other groups.

Figure 3. Length of stay of study groups by admission type.



The total direct cost estimate was highest in children below 5 years old with a mean of 52034.19 (CI 49473.80 - 54594.58) MNT, and total indirect cost was highest among pregnant women with the mean of 140491.90 (CI 120021.10 - 160962.60) MNT. However, pregnant women had less direct costs with the mean of 44482.46 (CI 41459.63 - 47505.29) MNT, and older people above 65 years old had less indirect costs of 36163.40 (CI 20947.31 - 51379.50) MNT compared with other groups.

Table 8. Total direct and indirect cost estimates of target groups (MNT).

Total direct cost	N	Mean	SE	95% Confidence Interval	
				Lower	Upper
Children below 5	951	52034.19	1304.68	49473.80	54594.58
Older people above 65	581	47631.26	1571.97	44543.83	50718.70
Pregnant women	583	44482.46	1539.08	41459.63	47505.29
Total indirect cost					
Children below 5	661	50314.33	3876.31	42702.95	57925.72
Older people above 65	73	36163.40	7632.99	20947.31	51379.50
Pregnant women	100	140491.90	10316.79	120021.10	160962.60

The total outpatient ILI per episode cost was estimated at 19.65 (18.53 – 20.77) USD and 31.73 (29.20 – 34.26) USD in SARI episodes. Whereas children below 5 years had the highest cost in outpatient episodes at 22.76 (20.61 – 24.92) USD, pregnant women had the highest cost in inpatient episode at 38.80 (30.38 – 43.22) USD.

Table 9. Outpatient and inpatient per episode costs by study population.

Study population	n	Mean		SE		95% Confidence interval			
						Lower		Upper	
Outpatient		MNT	USD	MNT	USD	MNT	USD	MNT	USD
Children				3122.8		58725.6			24.9
below 5	541	64860.07	22.76	5	1.10	6	20.61	70994.48	2
Older people				1820.5		42381.2			17.3
above 65	447	45959.19	16.13	7	0.64	3	14.87	49537.16	9
Pregnant				3046.4		49668.9			21.6
women	483	55654.80	19.53	1	1.07	2	17.43	61640.68	3
	1,47			1624.9		52792.1			20.7
Total	8	55979.59	19.65	4	0.57	6	18.53	59167.01	7
Inpatient									

Children below 5	506	93143.54	32.69	4880.66	1.71	83554.64	29.32	102732.40	36.06
Older people above 65	134	68156.21	23.92	5284.03	1.85	57704.60	20.25	78607.82	27.59
Pregnant women	119	104858.80	36.80	9236.16	3.24	86568.66	30.38	123148.90	43.22
Total	766	90408.17	31.73	3669.84	1.29	83204.01	29.20	97612.32	34.26
One ILI episode									
Children below 5	1,056	78354.44	27.50	2866.45	1.01	72729.85	25.53	83979.03	29.47
Older people above 65	592	51205.56	17.97	1886.81	0.66	47499.90	16.67	54911.22	19.27
Pregnant women	606	65977.66	23.16	3168.86	1.11	59754.36	20.97	72200.96	25.34
Total	2,273	67737.72	23.77	1669.37	0.59	64464.08	22.62	71011.37	24.92

Household wealth classification

Household monthly and quarterly consumption data were used to estimate monthly household consumption. Quarterly consumption variables were divided by three to get monthly estimates. Once monthly estimates were calculated, the remaining variables were summed. According to the National Bureau of Statistics, the average wage was 1,700,382 MNT (596.8 USD) in the urban area and 1,471,851 MNT (516.6 USD) in the rural area. Furthermore, those who earned 40% (2,380,535 - 2,720,611 MNT [835.48 - 954.84 USD]) higher than average wages were classified as upper middle class and those who earned 60% (2,720,612 MNT [954.84 USD]) and above were counted as upper class. Conversely, people who earned 40% (1,020,229 - 680,153 MNT [680,152 USD]) lower than the average wage were classified as low-income class and those who earned 60% and below were counted as near poverty class.

Table 10. Study population by geographic area.

Geographic area	Children below 5		Older adults above 65		Pregnant women	
Urban	n	%	n	%	n	%
Near poverty	168	27.86	139	37.47	124	38.51
Low income	179	29.68	105	28.3	90	27.95
Middle class	228	37.81	111	29.92	97	30.12
Upper middle class	6	1	3	0.81	3	0.93
Upper class	22	3.65	13	3.5	8	2.48
Total	603	100	371	100	322	100
Rural						
Near poverty	164	26.49	154	38.02	106	23.93
Low income	147	23.75	117	28.89	114	25.73
Middle class	271	43.78	121	29.88	179	40.41
Upper middle class	18	2.91	5	1.23	16	3.61
Upper class	19	3.07	8	1.98	28	6.32
Total	619	100	405	100	443	100

Economic burden of illness

When estimating households affected by the ILI episode, near-poverty classes had the highest economic impact and there were significant differences in the effect on households based on their wealth classification.

Table 11. Household wealth and economic burden.

Household wealth	Cost of illness exceeded 25% of monthly income	
	No	Yes

Urban	n	%	n	%	P value
Near poverty	298	68.0	140	32.0	
Low income	291	77.2	86	22.8	
Middle class	330	74.8	111	25.2	
Upper middle class	7	58.3	5	41.7	0.027
Upper class	33	75.0	11	25.0	
Total	959	73.1	353	26.9	
Rural					
Near poverty	265	61.8	164	38.2	
Low income	309	81.3	71	18.7	
Middle class	476	82.6	100	17.4	
Upper middle class	34	85.0	6	15.0	0.001
Upper class	46	82.1	10	17.9	
Total	1,130	76.3	351	23.7	

Among the study participants, 351 (50.4%) of those who were diagnosed with the influenza and pneumonia had more economic burdens (p<0.001).

Table 12. Economic burden by International Classification of diseases-10.

ICD classification	**Cost of illness exceeded 25% of monthly income**				
	No		**Yes**		**Total**
Acute upper respiratory infections	714	34.2%	156	22.4%	870
COVID-19	68	3.3%	83	11.9%	151
Chronic lower respiratory disease	31	1.5%	12	1.7%	43
Influenza and pneumonia	900	43.1%	351	50.4%	1,251
Lung diseases due to external agents	2	0.1%	1	0.1%	3
Other acute lower respiratory diseases	364	17.4%	91	13.1%	455

Other diseases of upper respiratory tract	9	0.4%	2	0.3%	11
Total	2,088	100.0%	696	100.0%	2,784

Compared to the other regions, households in Khangai region had the highest burden 24 (24.7%) among outpatient, and West region households had the highest burden 64 (55.7%) among inpatient per episodes. Overall, Khangai and West regions had significantly higher proportions of households experiencing catastrophic costs occurred by ILI/SARI compared to the Capital, Central, and Eastern regions.

Table 13. Economic burden by residential location.

Geographic area	**Cost of illness exceeded 25% of monthly income**				
	No		**Yes**		
Outpatient	n	%	n	%	P value
Capital	636	79.1	168	20.9	0.001
Central	360	83.9	69	16.1	
East	178	92.7	14	7.3	
Khangai	73	75.3	24	24.7	
West	151	79.1	40	20.9	
Total	1,398	81.6	315	18.4	
Inpatient					
Capital	371	65.0	200	35.0	0.001
Central	142	70.7	59	29.4	
East	85	75.2	28	24.8	
Khangai	27	50.9	26	49.1	
West	51	44.4	64	55.7	
Total	676	64.2	377	35.8	

Annual burden of ILI and SARI

A total of 557,984 outpatient visits and 88,731 visits were reported at the surveillance sites in the 2021–22 influenza season. Furthermore, in the last five influenza seasons excluding 2020–21, an average of 401,922 ILI visits and 47,393 SARI cases were reported at the national level. By multiplying the current season of ILI/SARI visits reported at the sentinel sites by per episode cost results, approximately 11 million USD (10,9 mln – 11,5 mln) from the ILI and 2,8 million USD (2,6 mln – 3 mln) from the SARI costs were incurred from healthcare services.

V. DISCUSSION

According to the previous WHO guidelines, it is recommended that the economic burden should not be benchmarked against the gross domestic product (GDP) because the economic burden provides an estimate of health-care spending and loss of productivity, while GDP is a domestic production function of society. There is no direct relation between the economic burden and GDP. Therefore, we did not express our findings using GDP.

This study found that households with children below 5 years old have a significantly higher risk of the catastrophic costs incurred by the ILI and SARI owing to indirect and direct costs in Mongolia. Therefore, households with lower wealth index are unable to afford medicines or consultation fees that are not covered by the NHI.

We have found that ILI per episode cost was 19.65 (18.53 – 20.77) USD and 31.73 (29.20 – 34.26) USD in SARI episodes. However, ILI per episode cost was estimated to be significantly higher than Mongolia at 88.09 USD among all age groups (Vo, 2017) in a study in Vietnam. Meanwhile, In Bhutan, influenza associated outpatient visit median per episode cost was estimated to be 4.22$ among public health providers and 8.59$ for private health providers, which can be considered as a relatively close result.

Moreover, from the societal perspective analysis, the annual economic burden was higher among ILI based on the greater number of ILI cases comparing to the SARI cases. However, ILI cases can be admitted as the SARI cases, which may further cause economic burdens for those households.

In addition to the study results, households located in the south eastern part of Mongolia had a higher economic burden during SARI and ILI cases. This could be owing to the higher cost of fuel, which places the market at the higher price compared to the other regions.

Our data collection is limited to the only influenza season in Mongolia from September to May. It does not reflect the full scope of the morbidity at the national level and the annual burden of ILI/SARI cases are limited to the sentinel sites. Therefore, indirect cost estimation is limited to absenteeism-related costs.

Further implication

Further study is needed not only to promote seasonal influenza vaccination but to plan and guide ILI and SARI responses. Current national regulations and standards suggest a modification of public health responses based on the ILI/SARI incidence. When using these indicators, the economic burden on households should be carefully considered.

Ethical considerations

Questionnaires and methods of this study received ethical clearance on 20th December 2019 by the Mongolian National University of Medical Sciences, Institutional Review Board approval № 2019/3-13.

VI. CONCLUSION AND RECOMMENDATION

The current study aimed to determine ILI and SARI per episode costs, economic burden among households, and annual out-of-pocket costs incurred by the patients and their caregivers. We chose three vulnerable groups for the seasonal influenza to determine the severity of the burden caused by illness.

All of the collected data were imported using specific codes without exposing the identity of the respondents. Direct and indirect medical and non-medical costs were summed by each individual and household consumption data used to define wealth classification.

Owing to the annual burden of ILI/SARI, Mongolian households experience significant socio-economic impacts due to catastrophic costs incurred as a result of illness. Despite the impact on the population, children below 5 years old had the highest direct cost and pregnant women had the highest indirect cost comparing to the other risk groups. The economic burden caused by illness affected low-income households adversely. Furthermore, near-poverty class households experienced catastrophic healthcare costs owing to ILI and SARI episodes.

Geographically, households in the West and Khangai region reported the highest proportion of economic burden in this study. An annual economic burden of the ILI/SARI, estimated to be approximately 11 million USD (10.9 mln – 11.5 mln) from ILI and 2.8 million USD (2.6 mln – 3 mln) from the SARI costs, were incurred owing to health care service.

We have found that during each ILI season, a substantial number of households experience socio-economic challenges owing to ILI and SARI. These results will be used as part of the evidence to further study cost-effectiveness of seasonal influenza in Mongolia to improve vaccination uptake and increase awareness of ILI/SARI prevention and treatment.

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APPENDICES

APPENDIX 1. Patient Questionnaire

Table 14

Data collectors code:			-			-				Responded ID
Hospital name:							Data collectors name:			
Date of survey y/m/day:					/			/		
Inpatient or Outpatient: □ Inpatient □ Outpatient										
Patient info										
1. Patient's study ID:							2. Patient's ID from hospital:			
3. Date of birth: / /							4. Patient's phone number:			
5. Patient's address:							6. Patient's other contact phone number:			
7. Height(см):			8. Weight(кг):				9. Gender: □male □female			
10. Pregnancy status: □yes □no							11. if yes, pregnancy month: ____________			
Clinical info										
12. Date of admission: / /							13. Date of discharge: / /			
14. Admission ICD10:							15. Last ICD10:			
16. Did patient have co-morbilities: □yes □no □don't know			17. If yes, how many co-morbilities? □Weakened immune system □Anemia □Kidney disease □Chronic obstructive pulmonary blockage □Rachitis □Dementia □Diabetes □Others ____________ □Others ____________ □Others ____________							
18. Outcome on discharge: □Healed, alive □Dead □Moved____________________ □Got well										
19. How many days/hours you stayed in each one (write down unit by unit): Outpatient clinic:_____ Pediatric ward:_____ Intensive care unit:_____ Isolation unit:_____ Emergency room:_____ Others..................................:_____										

20. Did patient take diagnostic tests during treatment? □Yes □No □Don't know

21. If yes write down which tests were taken and how many times each test was taken:

Virusology tests:	Blood tests:	*Radiology*
Rapid influenza test ____	HCT/PCV ____	*CT scan* ____
PCR influenza test ____	Blood chemistry ____	*Ultrasound* ____
Other influenza test............ ____	HIV ____	*Other X-ray* ____

Out of pocket patient survey

22. Number of days of illness before this clinic visit ______

23. What kind of symptoms you had?
□Fever >38C ____degree ____ days □Cough
□Sore throat □Felt feverish □Others______________

24. Did you receive care before arriving at this facility? □Yes □No □Don't know

25. Which one was the **first** place you went? (Skip if you didn't seek treatment before)
□Traditional healer □Pharmacy □Public clinic □Health center
□Private hospital □Family health center □Other_______________

26. What was the total cost of services there? /Tugrik/

Consultation		Medicine		Telephone	
Transport		Diagnosis		Food	
Бусад.........................					

27. How many relatives or caregivers accompanied you for this visit? _____________

28. Write down the number of days each caregiver or relativespent					
	What connection do you have?(uncle, aunt, mom, dad, etc.)				
	Days of accompanied with you				

29. Which was the **second** place you went? (Skip if didn't seek treatment before)
□Traditional healer □Pharmacy □Public clinic □Health center
□Private hospital □Family health center □Other_______________

30. What was the total cost of services there?/Tugrik/

Consultation		Medicine		Telephone	
Transport		Diagnosis		Food	
Other.........................					

31. How many relatives or caregivers accompanied you for this visit? _____________

32. Write down the number of days each caregiver or relative spent					
	What connection do you have?(uncle, aunt, mom, dad, etc.)				

	Days of accompanied with you				

33. Which was the **third** place you went. /Skip if you didn't seek before/
□Traditional healer □Pharmacy □Public clinic □Health center
□Private hospital □Family health center □Other____________

34. What was the total cost of services there? /Tugrik/

Consultation		Medicine		Telephone	
Transport		Diagnosis		Food	
Other.........................					

iiii35. How many relatives or caregivers accompanied you for this visit? ___________

36. Write down the number of days each caregiver or relative spent	What connection do you have?(uncile, aunt, mom, dad etc.)				
	Days of accompanied with you				

Patient transportation info

37. How long did it take to get here from patient home (including the journey time and any waiting for transport)? _____hours_____minute

38. What kind of transportation did the patient use to this hospital or clinic? (write down duration of transport and cost)
□Car ______Min_________Tugrik □Bus ______Min_________Tugrik
□Ambulance ______Min_________Tugrik □Taxi ______Min_________Tugrik
□Foot ______Min_________Tugrik □Other( ) ______Min_________Tugrik

Treatment costs

39. How much did you actually have to pay for medicine and like services? (Tugrik)

	Medicine	Diagnosis	Consultation	Other
Total cost				
Discounted cost of insurance				
Individual expenditure				

Absenteeism

40. Do you go to school/work regularly? □Yes □No

41. Has the illness affected the family financially? □Yes □No □Don't know □No response

42. How did you pay costs related to these services (write costs behind)?
□Don't know

□ Reduced other costs	______tugrik	□ Donation from relatives	______tugrik
□ Savings	______tugrik	□ Others___________	______tugrii

□ Borrowings	______ tugrik	□ Others______	______ tugrik

43. How many visits did you get during sickness?

Your relation					
How many times					
Cost per visit					

44. Family member numbers: Adult_________ Kids_________

45. Total household income per month? _____________

46. How many people have a monthly income in your household? ___________

HOUSEHOLD CONSUMPTION /tugrik/

	Type of expenditure	Average in month	Average in last 3 months
Household food consumption	Flour		
	Bakery		
	Meat		
	Meat products		
	Milk		
	Milk products		
	Vegetable		
	Oil		
	Fruit and sweets		
	Alcohol		
	Tobacco		
	Tea, juice		
	Other items not mentioned above		
Non-food consumption	Clothing		
	School uniform		
	Health /consultation, others/		
	Transportation /fuel, maintenance etc./		
	Vacation		
	Furniture /procurement, rent etc./		
	Sanitary products /soap, toothpaste etc./		
	Other items not mentioned above		
Housing use	Area fee /rent etc./		
	Condominium association /heating, water etc./		
	Electricity		
	Fuel /wood, coal, gas etc./		

	Maintenance			
	TV, radio, internet			
	Phone			
	Others /sanitation etc./			
Others	Money spent for non-family members			
	Education fee /preschool/			
	Medicine, treatment costs			
	Holiday /new year etc./			
	Settlement costs			
	Unexpected costs /wedding, funeral etc./			

APPENDIX 2. Caregiver questionnaire

Data collectors code: ☐☐ - ☐☐ - ☐☐☐	Responded ID
Hospital name:	Data collectors name:
Date of survey y/m/day: ☐☐☐☐ / ☐☐ / ☐☐	

Caregiver info

1. Relationship with the patient
☐Mother ☐Father ☐Sister ☐Brother ☐Grandfather ☐Grandmother
☐Child ☐Friend ☐Relative ☐Other

2. Education level: ☐None ☐Low ☐Elementary ☐Secondary ☐University ☐Others

3. How many people cared for the patient during his/her illness (numbers)? _________

Caregiver(s) transportation info
Interview only one caregiver about their costs.

4. Did you came here with the patient? ☐Yes ☐No

5. What kind of transportation did the caregiver use to this hospital or clinic? (Write costs behind)
☐Car __________tugrik ☐Bus __________tugrik ☐Ambulance__________tugrik
☐Taxi __________tugrik ☐Foot __________tugrik
☐Other(______________)__________tugrik

6. Please write one-way cost? (in Tugrik)?

Missed work and lost income

7. Do you work? ☐Yes ☐No ☐Retired

8. Occupation status?
☐Entrepreneur ☐Home retail ☐Farmer ☐Seasonal work
☐Household production ☐Government sector ☐Private sector ☐Other

9. Your monthly income: ____________________ tugrik

10. How many days have you been absent from work? Total:______________ Paid leave:_______________

11. Total household income: ______________________ tugrik

12. Did you borrow money with interest to cover patient's health expenditure? ☐Yes ☐No

If yes, did you repay your loan? ☐Yes ☐No

13. If no, after how many years do you need to repay your loan?
☐<1 year ☐1-3 year ☐3-5 year ☐5+ year ☐Don't know ☐ No response

14. How are you going to repay your loan?
☐Working overtime ☐Sell assets ☐Get other loan ☐Reduce food consumption
☐Reduce education costs ☐Others (_________________)

15. Will you go back to work immediately? ☐Yes ☐No

16. If not, how many days will you lose? ______________

17. If there were other caregivers, how many days did they lose? And how much income? (responding caregiver not included)

Relationship with patient					
Days spent with patient					
Lost income					

APPENDIX 3. Follow-up questionnaire

(7 days after hospital discharge and 14 days after discharge)

Data collectors code:			-			-				Responded ID

Hospital name:	Data collectors name:

Date of survey:					/			/		

Patient info

1. Patient study ID: ☐☐☐☐☐☐☐☐☐☐

2. Contact phone number: ☐☐☐☐☐☐☐☐

3. Discharge date? ☐☐☐☐ / ☐☐ / ☐☐

Transportation info

4. What kind of transportation did you use to go home from hospital or clinic? (Write down costs)
□Car __________tugrik □Bus __________tugrik □Ambulance__________tugrik
□Taxi __________tugrik □Foot __________tugrik □Other(_______)_______tugrik

Treatment costs

5. Did you get a home-visit as an outpatient? □Yes □No □Don't know
If yes, how many times? ____________________

6. Did you contact any health facility seeking for care after you went home?
□Yes □No □Don't know

10. If yes, which one is it?
□Traditional healer □Pharmacy □Public hospital □Health center
□Private hospital □Family health center □Other____________

11. If yes, how much did you pay for these?

Consultation		Medicine		Telephone	
Transportation		Diagnosis		Food	
Others..........................				**TOTAL**	

12. How many caregivers accompanied you for this visit? ___________

13. How many days did caregivers accompany you *(Write days accompanied with you)*	Your relation with caregiver				
	Number of days accompanied				

16. If you are a student, how many days of school have you missed since returning from the clinic?
____

17. Are you still taking medication for the flu? □Yes □No
18. Are you back at work/school? □Yes □No

19. Are you healed completely? □Yes □No □Don't know

Thank you for participating
2nd week follow-up survey

Treatment cost
6. Did you contact any health facility seeking for care after you went home? □Yes □No □Don't know
10. If yes which one was it? □Traditional healer □Pharmacy □Public hospital □Health center □Private hospital □Family health center □Other ______________
11. If yes, how much did you pay for these?

Consultation		Medicine		Telephone	
Transportation		Diagnosis		Food	
Others.........................				**TOTAL**	

12. How many caregivers accompanied with you for this visit?____________

13. How many days did caregivers accompany you *(Write days accompanied with you)*	Your relationship with caregiver				
	Number of days accompanied				

16. If you are a student, how many days of school have you missed since returning from the clinic? __________
17. Are you still taking medication for the flu? □Yes □No 18. Are you back at work/school? □Yes □No 19. Are you healed completely? □Yes □No □Don't know