ECONOMIC LOSS OF ACUTE GASTROENTERITIS ON HOUSEHOLDS IN MALAYSIA AND ITS ASSOCIATED FACTORS

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UNIVERSITI SAINS MALAYSIA

2020

ECONOMIC LOSS OF ACUTE GASTROENTERITIS ON HOUSEHOLDS IN MALAYSIA AND ITS ASSOCIATED FACTORS

By

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Research Project Report submitted in partial fulfilment of the requirement for the degree of Master of Public Health

JUNE 2020

ACKNOWLEDGEMENTS

In the name of Allah, the Most Compassionate, the Most Merciful. Salutation is upon His Messenger Muhammad S.A.W., his family and his companions. I would like to extend my deepest gratitude and thanks to the following individuals who have contributed and supported me during the preparation of this dissertation.

1. Dr Surianti binti Sukeri, my supervisor and lecturer from Department of Community Medicine, School of Medical Sciences, Universiti Sains Malaysia (USM).

2. Associate Professor Malina binti Osman, my co-supervisor from Department of Medical Microbiology and Parasitology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia (UPM).

3. All of my lecturers from Department of Community Medicine, School of Medical Sciences, Universiti Sains Malaysia who have given me guidance and support.

4. My fellow colleagues from Master of Public Health.

5. My dear husband, Mohd Fadhil Azrie bin Yahya, my parents; Jusoh bin Omar and Siti Norbe binti Anas, and my siblings for their endless encouragement and prayers.

Collaboration

This study was part of a larger research project entitled 'Strategic Integrated Measure on Advocating IDEAS2: A Comprehensive Fundamental, Technical and Public Health Approaches' funded by the Malaysian Research University Network (MRUN) grant in collaboration with UPM, UNISZA, UMS and USIM. However, I conducted all data collection and analysis pertaining to this study.

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LIST OF ABBREVIATIONS

AGE	Acute gastroenteritis
CI	Confidence interval
DOSM	Department of Statistics Malaysia
FBD	Foodborne Diseases
HSNZ	Hospital Sultanah Nur Zahirah
MOH	Ministry of Health
NHMS	National Health Morbidity Survey
SD	Standard deviation
UMMC	University of Malaya Medical Centre
WHO	World Health Organisation

ABSTRAK

Latar belakang: Gastroenteritis akut (AGE) mengakibatkan kesan yang signifikan terhadap kesihatan dan ekonomi di Malaysia. Beban ekonomi tersebut tidak hanya mempengaruhi penyedia perkhidmatan kesihatan, tetapi juga kewangan isi rumah. Kajian dalam komuniti tentang kerugian kewangan isi rumah akibat AGE adalah penting kerana majoriti individu yang terjejas tidak mendapatkan rawatan yang formal.

Objektif: Kajian ini dijalankan untuk mengkaji kerugian ekonomi yang disebabkan oleh AGE dalam kalangan isi rumah di Malaysia dengan menganggarkan; 1) kos perubatan langsung, 2) kos bukan perubatan langsung dan 3) kos tidak langsung dan untuk menentukan faktor-faktor yang berkaitan dengan jumlah kerugian ekonomi isi rumah.

Kaedah: Kajian keratan lintang ini dijalankan dari Disember 2019 sehingga Mac 2020 menggunakan proforma kos dwibahasa yang telah diedarkan melalui tinjauan berasaskan web berbayar (Survey Monkey) dalam kalangan individu yang melaporkan sendiri AGE di Malaysia. Analisis deskriptif dan regresi linear telah dijalankan.

Keputusan: Secara keseluruhan, purata kerugian ekonomi isi rumah akibat satu episod AGE tanpa mengira penggunaan perkhidmatan kesihatan adalah RM406.37 (± SD 885.73) dengan kos langsung sebanyak RM147.23 (± SD 703.09) dan kos tidak langsung sebanyak RM259.14 (± SD 379.92). Kos adalah tertinggi dalam kalangan orang yang mendapat rawatan di hospital, diikuti oleh orang yang mendapat rawatan di klinik dan paling rendah dalam kalangan orang yang tidak mendapatkan rawatan. Kami turut mendapati bahawa kos tidak langsung adalah lebih tinggi dari jumlah kos langsung. Analisis regresi linear berganda menunjukkan bahawa jumlah pendapatan

isi rumah (RM0.14; 95% CI: 0.01, 0.27; p=0.043) dan jenis fasiliti (kerajaan atau swasta) (RM1842.05; 95% CI: 395.13, 3288.98; p=0.014) mempunyai kaitan yang signifikan yang dengan jumlah kerugian ekonomi isi rumah.

Kesimpulan: Gastroenteritis akut mengakibatkan kos yang besar terhadap semua isi rumah yang terlibat tanpa mengira penggunaan servis kesihatan. Penyumbang utama kerugian ekonomi adalah kos tidak langsung (kehilangan produktiviti) yang berdasarkan bilangan hari tidak bekerja. Oleh itu, AGE telah membebankan kedua-dua ekonomi isi rumah dan majikan. Hal ini menunjukkan bahawa banyak sumber dapat dijimatkan melalui pecegahan dan promosi kesihatan AGE. Di samping itu, jumlah pendapatan isi rumah dan jenis fasiliti adalah faktor-faktor yang signifikan bagi jumlah kerugian ekonomi isi rumah akibat AGE. Hal ini menunjukkan bahawa pembiayaan kesihatan di Malaysia bersifat progresif dan saksama kerana orang berpendapatan lebih tinggi membayar kos yang lebih tinggi; tetapi pada masa yang sama, kawalan terhadap bayaran rawatan di fasiliti kesihatan swasta adalah diperlukan.

KATA KUNCI:

Gastroenteritis akut, isi rumah, kerugian ekonomi, kos langsung, kos tidak langsung

ABSTRACT

Background: Acute gastroenteritis (AGE) imposes significant health and economic burden in Malaysia. The economic burden affects not only healthcare providers but also households' finances. A community survey on the household financial loss due to AGE is warranted since the majority of affected individuals did not seek formal treatment.

Objective: To study the economic loss attributable to AGE among households in Malaysia by estimating; 1) the direct healthcare, 2) direct non-healthcare and 3) indirect costs and to determine associated factors for total households' economic loss.

Methodology: A cross-sectional study was conducted between December 2019 and March 2020, using a bilingual costing proforma which was distributed using a paid web-based survey (Survey Monkey) among individuals with self-reported AGE in Malaysia. Descriptive analysis and linear regression were applied.

Results: Overall, the average total households' economic loss due to a single episode of AGE regardless of their utilisation of healthcare services was RM406.37 (± SD 885.73) with direct cost RM147.23 (± SD 703.09) and indirect cost RM259.14 (± SD 379.92). The cost was the highest among those who obtained inpatient care, followed by outpatient care and the least was among those who did not seek treatment. We also observed that the indirect cost was higher than the total direct cost. The multiple linear regression analysis showed that the total household income (RM0.14; 95% CI: 0.01, 0.27; p=0.043) and type of facility (private vs government) (RM1842.05; 95% CI: 395.13, 3288.98; p=0.014) had a significant association with the total households' economic loss.

Conclusion: Acute gastroenteritis had incurred substantial cost on all affected households regardless of their utilisation of healthcare services. Interestingly, the main cost driver for the economic loss was the indirect cost (productivity loss) based on days away from work. Therefore, AGE had caused economic burden on both households and employers. It signifies that a tremendous amount of resources can be saved by prevention and health promotion of AGE. In addition, the total household income and type of facility were found to be significant factors associated with the total households' economic loss due to AGE. It shows that healthcare financing in Malaysia is progressive and equitable as the richer pay higher cost; but at the same time, a greater control over private healthcare fees is warranted.

KEYWORDS:

Acute gastroenteritis, households, economic loss, direct cost, indirect cost

CHAPTER 1

INTRODUCTION

1.1 Background

1.1.1 Burden of acute gastroenteritis

Acute gastroenteritis (AGE) is caused by the inflammation of mucus membranes in the gastrointestinal tract and is presented by diarrhoea and vomiting (Chow *et al.*, 2010). It can present with other symptoms including abdominal pain, nausea and fever (Catherine and Aftab, 2012).

Globally, there are approximately 1.7 billion cases of childhood diarrhoea every year. Diarrhoea kills 2195 children daily, making it the second leading cause of death among children under five years; especially among those who live with HIV, have impaired immunity and are malnourished (CDC, 2015; WHO, 2017). The morbidity and mortality are mostly due to poor water sources and contaminated food. A large three-year, prospective study at seven sites in African and Asia reported that the odds of mortality during the follow-up among patients with moderate-to-severe diarrhoea was 8.5 higher compared to the controls (Kotloff *et al.*, 2013).

In low-income countries, there is a vicious cycle where diarrhoea can result in malnutrition and malnourished children are then more susceptible to another episode of diarrhoea. This disruption of physical development in early years can lead to impaired cognitive function as those period are the critical phase of development (MacIntyre *et al.*, 2014).

In Malaysia, Loganathan *et al.* (2016) estimated that approximately 61 deaths, 70,000 hospitalisations and 193,000 outpatient visits which related to AGE among children under five-year-olds in 2013. The rotavirus infection accounted for almost half of these mortality and morbidity. Another study estimated a lower number of hospitalisations of 13,936 (Hsu *et al.*, 2005). The usage of different data source from different years might explain the discrepancy between these estimations. Loganathan *et al.* (2016) used data from both private and government hospitals, together with the estimation of unreported cases from 2011 and 2013. On the other hand, Hsu *et al.* (2005) used data from government hospitals alone between 1999 and 2000.

Data on the burden of AGE among older children and adults remain sparse in Malaysia, similar to the global situation (Lopman, 2016). National estimates of diarrhoeal morbidity and mortality were produced annually for 195 countries, including Malaysia, as a part of the Global burden of Diseases, Injuries and Risk Factors Study 2015 (GBD 2015). It reported that Malaysia had 385 deaths and 28305 DALYs attributable to diarrhoeal disease in all ages (Troeger *et al.*, 2017). A Malaysian population-based study reported 5.0% four-week incidence of acute diarrhoea and the highest incidence was among young adult aged 20-29 years (Gurpreet *et al.*, 2011).

1.1.2 Cost-of-illness

Cost-of-illness measures the economic loss attributable to illness. Its data serves many purposes such as to communicate the weight of the health problem to the policymakers, provide information on potential benefits if intervention is done and allow comparison between countries (Jo, 2014).

The cost-of-illness study can be done either by retrospective or prospective approaches. The retrospective approach is when data is collected once an event has already occurred. In contrast, information is collected by following patients over a period of time in the prospective approach. The significant advantages of the retrospective approach are it is less costly and time-saving (Jo, 2014).

Measuring the cost-of-illness can be carried out from various perspectives such as from households, providers or societal views (McLinden *et al.*, 2014). A review by Jo (2014) listed broader cost-of-illness perspectives such as societal, healthcare system, third party payer, business, government and household. Each perspective uses different cost components, which will yield diverse results for the same illness. Nonetheless, each perspective provides valuable information to the specific group.

1.1.3 Economic loss of acute gastroenteritis

There is a significant economic loss accompanying AGE morbidity and mortality. For instance, a population-based cohort study in Sweden showed the incidence of AGE was 360/1000 person-year. It caused €1 billion economic loss annually and almost 9 billion days away from work and school (Edelstein *et al.*, 2016). In Southern Asia

countries such as Bangladesh, the average total societal cost-of-illness per episode was USD67.18. The burden was the highest for the poorest households (Sarker *et al.*, 2018).

Our local data showed the cost to treat hospitalised childhood AGE ranged from USD34-350 per episode per person (Lee *et al.*, 2012; Loganathan *et al.*, 2015). According to an estimation using multiple data resources in 2016, rotavirus gastroenteritis was estimated to cost USD34 million to the healthcare provider and USD50 million to society in Malaysia (Loganathan *et al.*, 2016).

1.2 Statement of problem

Acute gastroenteritis imposes a significant health and economic impact in Malaysia. The economic burden of AGE affects not only healthcare providers but also afflicting families' finances, especially those who are at the edge of poverty. Several studies had been conducted in Malaysia to estimate the households' economic loss attributable to AGE in hospital setting. However, majority of individuals with AGE do not seek treatment in healthcare facility because of its mild presentation. Therefore, these studies provide incomplete representation of the actual burden. To our knowledge, there is no nationwide and comprehensive bottom-up households' economic costing regardless of their health-seeking activities in the community on all age groups.

1.3 Rationale

The economic loss of AGE from households' perspective is one of the components required to determine the cost-of-illness of AGE in Malaysia. The lack of accurate data on the economic loss of a disease will cause difficulties in resource allocation as there is no scientific data to direct where the resource should be prioritised. Therefore, this study serves a few purposes. Firstly, findings from this study may act as supporting data for future cost-effectiveness study on AGE interventions. Secondly, it illustrates the magnitude of AGE-related complications beyond the scope of healthcare to the policymakers. Thirdly, the data can be used for international comparison in estimating the global burden of AGE.

Since most patients with AGE do not seek treatment, they are more likely to be in the community setting rather than at healthcare facilities. Therefore economic costing should also be done in the community instead at hospital or outpatient setting to obtain more coverage and accurate cost burden of AGE.

Further, factors associated with the total household economic lost was also minimally explored in the past. The only factors that were ever studied in Malaysia were income status, residential area and presence of rotavirus infection. In this study, additional factors were analysed. The data on economic loss arising from any illnesses is crucial as it may affect households' expenses thus shaping their health-seeking activities. For example, households with higher costs will probably defer treatment due to their financial constraints and subsequently endanger their life. High economic loss may also cause households to reduce expenditure on other activities such as food or education.

1.4 Research questions

1. From a household perspective, what are the direct healthcare and non-healthcare costs due to acute gastroenteritis in Malaysia?
2. What is the estimated indirect cost attributable to acute gastroenteritis among households in Malaysia?
3. What are the factors associated with total households' economic loss in view of acute gastroenteritis?

1.5 Objectives

1.5.1 General objective

To study the economic loss due to acute gastroenteritis among households in Malaysia.

1.5.2 Specific objectives

1. To estimate the direct healthcare and non-healthcare costs due to acute gastroenteritis among households in Malaysia.
2. To estimate the indirect cost attributable to acute gastroenteritis among households in Malaysia.
3. To determine the associated factors for total households' economic loss in view of acute gastroenteritis in Malaysia.

1.6 Research hypothesis

$H_{A:}$ There is significant socio-demographic, episode of illness and patient seeking activities factors associated with total households' economic loss of acute gastroenteritis in Malaysia.

CHAPTER 2

LITERATURE REVIEW

2.1 Acute gastroenteritis

The case definition of AGE varies from one study to another, even though they are trying to evaluate the same phenomenon. A study among elderly in Australia defined AGE as ≥3 loose stools and/or ≥1 episode of vomiting within 24 hours, excluding non-infectious cause (Kirk *et al.*, 2012). In contrast, Edelstein *et al.* (2016) defined AGE as ≥3 episodes of loose stool or vomiting in 24 hours; or loose stool or vomiting with ≥2 other symptoms which include fever, nausea, vomiting and abdominal pain. Whereas another study defined AGE as ≥3 episodes of loose stool in 24 hours or vomiting which last more than a day and excluding those who had a cough or sore throat (Cantwell *et al.*, 2010). These examples demonstrated that definitions of AGE differ in term of the type of symptoms, frequency of symptoms per day, duration of symptoms and exclusion criteria.

Due to the lack of a standard AGE definition, a large population-based study in five countries including Australia, Canada, Ireland, Malta and the United States suggested a standardised AGE definition of ≥3 loose stool or any vomiting within 24 hours. This illness should not be related to chronic disease of the bowel (bowel cancer, ulcerative colitis and Crohn's disease), pregnancy, alcohol or drug intake (Majowicz et al., 2008). In this present study, we modified the definition of AGE as recommended by Majowicz *et al.* (2008). We defined a case of AGE as someone who had ≥ 3 loose stool and/or ≥ 3 vomiting within 24 hours.

The WHO (2017) defined diarrhoeal disease as the passing of ≥3 loose stool or liquid stool per day (or more frequent passage than usual for the individual). The term AGE and diarrhoeal disease are sometimes used interchangeably because they are explaining an almost identical clinical phenomenon. For example, Glasgow *et al.* (2013) and Loganathan *et al.* (2015) used the WHO definition for diarrhoeal disease in defining an AGE case in their studies. Generally, the difference between the definition of AGE by Majowicz *et al.* (2008) and diarrhoeal disease by the WHO (2017) is the inclusion of vomiting in the term AGE. Since these terms can be overlapping, studies on the diarrhoeal disease will also be explored.

Chow *et al.* (2010) stated that virus accounts for approximately 70% of AGE. The most common virus causing this disease worldwide is rotavirus. Other viruses include adenovirus and astrovirus. A bacterial infection such as *Salmonella* species, *Campylobacter* species, *Shigella* species and *Yersinia* species are responsible for 10% to 20% of all AGE cases. On the other hand, *Giardia lamblia* is the most common protozoal infection which causes persistent diarrhoea. Another study revealed that the most common pathogens detected were rotavirus, norovirus and *Salmonella* species (Bresee *et al.*, 2012). However, an etiologic agent is rarely identified because samples are not routinely obtained or limited ability of laboratories to detect a broad range of pathogens (Pont *et al.*, 2008).

As mentioned before, rotavirus is the most common cause of AGE, but it is also the leading cause of severe dehydrating diarrhoea in children worldwide, especially in developing countries (Widdowson *et al.*, 2009). In 2009, the WHO recommended for rotavirus vaccine; named Rotarix® or RotaTeq® in the national

immunisation program. However, up until 2017, only eight countries in Asia introduced the vaccine in their routine immunisation schedule (Burnett *et al.*, 2018). A systematic review by Lamberti *et al.* (2016) showed that the rotavirus vaccine is effective in preventing rotavirus diarrhoea and rotavirus hospitalisation among children under five years globally. The efficacy was 88.4% (95% CI 67.1-95.9%) in Southeastern Asia. In Malaysia, the vaccines are available in the private market but not in the routine schedule. The expensive vaccine becomes a barrier to the vaccine introduction in the national immunisation programme (Loganathan *et al.*, 2016). Besides, data on the magnitude of the problem is not extensive enough to inform policymakers to assess its potential value of vaccination.

Acute gastroenteritis is also associated with foodborne diseases (FBD). According to the Case Definition of Infectious Disease Third Edition by Ministry of Health Malaysia, the clinical case definition of food poisoning is an acute onset of vomiting and/or diarrhoea and/or other symptoms which is related to food ingestion (MOH, 2017). Therefore, the case definition also mimics the definition of AGE with the inclusion of diarrhoea and/or vomiting. This is supported by a study done by Hall *et al.* (2005), who reported that foodborne pathogens caused almost a third of AGE cases. It was estimated that among 4.6 million AGE cases with known pathogens, 1.5 million cases were foodborne. *Escherichia coli*, norovirus, *Campylobacter* species and *Salmonella* species caused 88% of these foodborne AGE cases.

In Malaysia, food poisoning cases are common because of the hot and humid climate, which is suitable for microorganism growth (Abdul-Mutalib *et al.*, 2015). The incidence rate of food poisoning from 2010 to 2013 had fluctuated between 44.2 to 56.3 per 100,000 population (MOH, 2014). The number was only the tip of an iceberg

as most cases did not seek treatment, and even if they did, it needed to undergo a complex chain of events before a foodborne case was officially logged (Soon *et al.*, 2011). Fifty percent of the FBD in Malaysia was caused by unsanitary food handling (MOH, 2007). Hence, a cost-of-illness on AGE will be valuable when evaluating the cost-effectiveness of intervention for FBD.

Similar to the global trend, contaminated water was a crucial factor associated with diarrhoea in Malaysia. Aziz *et al.* (2018) reported that children who used boiled, chlorinated or filtered water are twice less likely to develop diarrhoea as compared to children who used untreated water. Despite the increment of national coverage of water supply from 80% in 1990 to 95% in 2000, the rural population still had less access to clean water supply compared to that of urban population (Ahmed *et al.*, 2014).

2.2 Households' economic loss of acute gastroenteritis

Households' economic loss due to AGE is categorised into direct, indirect (productivity loss) and intangible cost. Direct costs are the direct payment made for medical purposes when healthcare is sought, and non-medical purposes such as transportation and accommodation. Indirect costs are productive time losses on the ill individuals or the caretaker, with no actual payment made. There are differences in the calculation whether to use average wage rate or actual income loss. Intangible cost is the non-monetary effect of pain and suffering attributable to the illness. It is seldomly quantified because of measurement difficulties (Filipovic *et al.*, 2011; McIntyre *et al.*, 2006).

Health events such as death or disease incur out-of-pocket (OOP) expenditure on households. A review by Alam and Mahal (2014) stated that significant OOP might push households to the edge of poverty, especially for those residing in low- and middle-income countries. Many strategies at the household level were identified to cope with this economic impact including using income, savings, borrowing, selling assets and making loans. The financial constraint can hinder individuals from seeking treatment and may put them in life-threatening situations. Therefore, inequalities exist in term of accessibility to treatment among different socio-economic groups.

Acute gastroenteritis undeniably had a substantial impact on the economy. Households cost due to AGE have been quantified in several different studies internationally. Majority of research on the cost-of-illness of AGE were done at hospital setting as it was convenient to obtain samples. On top of that, these studies focused on children under five-year-olds because of their vulnerability to AGE.

Burke *et al.* (2013) reported 45% of families in Bolivia paid more than one percent of their annual income for only an episode of paediatric AGE, while 1.9% of these families had spent more than 10% from their annual income. It demonstrated that families could experience a tremendous burden from a single AGE episode. Findings in high-income countries such as Canada estimated the parental cost of rotavirus in children under three years old in an Emergency Department in Canada was C$53.75 per episode (Saux *et al.*, 2012). The components of this parental cost were diapers, parking, travel costs and workdays lost related to AGE. Together with healthcare provider cost, it contributed to a societal cost of C$110.48 per episode. This data demonstrated the severe economic impact of AGE and set baseline data for the comparison before and after the rotavirus vaccine implementation in both countries.

The mean costs for all health-seeking activities for childhood diarrhoea were USD1.82, USD3.33 and USD6.47 in Bangladesh, India and Pakistan respectively (Rheingans *et al.*, 2012). While in another study in Bangladesh, the household cost for treating hospitalised diarrhoea patients were USD53.23 (Sarker *et al.*, 2018). There was cost discrepancy between these two studies in Bangladesh since the former study explored costs in all care-seeking activities, but the latter study focused only on hospitalised cases. It might also be influenced by the small sample size (n=95) and power in the former study. In Southeast Asia, a study in Thailand reported the OOP of rotavirus diarrhoea was USD370.38, corresponding to 40% of the total economic impact (Rochanathimoke *et al.*, 2019). However, this study excluded productivity loss as the patients were not at working age. This approach was an uncommon practice as majority studies counted productivity loss based on parental loss of wages due to days away from work while taking care of their sick children.

In Malaysia, the majority of cost-of-illness studies followed the international trend where they focused on paediatric AGE in hospital settings. Lee *et al.* (2012) reported the median direct and indirect cost of admitted paediatric diarrhoea patients in a university hospital (University Malaya Medical Centre, UMMC) and a private hospital in Kuala Lumpur (Selangor Medical Centre) was USD252.86. The cost for a single episode of admission represented 16% of the households' monthly income. Parents also reported experiencing negative impact such as feeling upset, burnout, lack of sleep and interruption of daily activities. This study proved that AGE posed severe implications on all three types of cost including direct, indirect and intangible costs. The limitation of this study was the sample was taken solely from Kuala Lumpur, a highly urbanised capital city in Malaysia. Consequently, they were unable to give an accurate picture of the economic burden of AGE among the urban, suburban and rural populations in Malaysia.

While in another study, Loganathan *et al.* (2015) stated the sum of direct and indirect cost for paediatric AGE was USD224 in Kuala Lumpur and USD35 in Kuala Terengganu. The massive difference was due to the type and location of the study setting; the UMMC in urban Kuala Lumpur versus a highly subsidised government hospital (Hospital Sultanah Nur Zahirah, HSNZ) in Kuala Terengganu. The missing data on direct hospitalisation charges in HSNZ also further underestimated the cost burden.

In view of most individuals affected with AGE do not seek treatment, a study to compare the cost of paediatric AGE between Malaysia and Vietnam was carried out outside health facility setting (Azmi and Reginald, 2015). The study sample was from residential and public areas in Hanoi and Bac Glang in Vietnam and Klang Valley,

Malaysia. The study revealed that the most common hospitalisation fees for paediatric gastroenteritis were more than USD350 in Malaysia, and ranged between USD1-USD34 in Vietnam. The cost was higher among study samples in Malaysia compared to that of Vietnam and other studies in Malaysia because the majority of children in this study were admitted to private hospitals. The limitation was the sample was obtained by convenience sampling in a single area (Klang Valley) in Kuala Lumpur and it only examined hospitalisation fees rather than comprehensive cost components.

Loganathan *et al.* (2016) estimated the societal economic loss of rotavirus gastroenteritis for the general population at USD50 million annually. A third of the societal cost was contributed by productivity loss. The study made a prediction based on multiple data resources including the available literature from a single healthcare facility (UMMC). The samples might not be representative of the whole country. It also focused only on one etiological agent named rotavirus.

Although several studies had been conducted in Malaysia to estimate the households' economic loss attributable to AGE, most of the studies revolved around hospitalised paediatric AGE cases only. There is no comprehensive bottom-up households' economic costing irrespective of their health-seeking activities on all age groups in various states in Malaysia.

2.3 Associated factors of households' economic loss

The main challenge faced by public health personnel is to identify associated factors that contribute to the households' economic loss. The only factors studied in our local setting were household income, residential area and presence of rotavirus infection. Whereas research in other countries included factors such as age, severity of illness and place of seeking care.

2.3.1 Household income

Rheingans *et al.* (2012) discovered that both direct and total household costs of AGE in Bangladesh, India and Pakistan were lower in the lowest wealth quintile. However, the authors considered the study finding as of marginal statistical significance; with p-value between 0.05 and 0.20 because of limited sample size and power. Similar findings were observed by Loganathan *et al.* (2015) which reported households in the highest income quintile had higher average OOP expenditure due to AGE (USD120 ± SD 179), followed by those in the lowest quintile (USD101 ± SD 66).

2.3.2 Residential area

The direct and indirect costs incurred for AGE on households were significantly higher in the urban area (USD224) compared to rural area (USD 35) (Loganathan *et al.*, 2015). This study compared a university hospital (UMMC) in Kuala Lumpur as a representative of the urban area and a public hospital (HSNZ) in Kuala Terengganu as a representative of the rural area. Loganathan *et al.* (2015) stated that the cost of living

in Kuala Terengganu was lower compared to that of Kuala Lumpur; thus the expenses by the households may be higher in the latter. However, it is worth to note that only half of Kuala Terengganu is rural area while another half is urban area. Therefore, Kuala Terengganu may not adequately represent the rural area.

2.3.3 Rotavirus versus non-rotavirus gastroenteritis

A study in Thailand obtained higher cost among patients with confirmed rotavirus cases compared to the non-rotavirus cases (Rochanathimoke *et al.*, 2019). The total of direct healthcare and direct non-healthcare cost on families for rotavirus cases was USD 337.28 compared to USD291.14 for non-rotavirus cases. The result was coherent with a study by Chai and Lee (2009) which reported that the direct and indirect costs were significantly higher in rotavirus cases compared to non-rotavirus cases (USD193.5 vs USD155.1). The difference may be explained by the extended hospital stays, higher hospital charges and more productivity loss. In contrast, there was no significant difference in direct and indirect cost between rotavirus and non-rotavirus cases in UMMC and HSNZ except for higher consultation cost pre-admission among rotavirus cases in HSNZ (Loganathan *et al.*, 2015).

2.3.4 Severity of illness

It was discovered that severe AGE was significantly associated with higher cost compared to mild and moderate form of illness (Rochanathimoke *et al.*, 2019). The study measured clinical severity of diarrhoeal episodes using Vesikari scale; which

incorporated the duration of diarrhoea and vomiting, number of loose stool and vomiting in 24 hours, maximal temperature recorded, hydration status and treatment received. Score ≥ 11 were grouped as severe, 7-10 were grouped as moderate, while ≤ 6 were grouped as mild (Ruuska and Vesikari, 1990). Rheingans *et al.* (2012) supported the findings as they found that there was a higher cost for moderate-to-severe acute diarrhoea (45%-50% higher) in Bangladesh and India as compared to the mild presentation. However, measuring severity is only appropriate in the healthcare setting, not in the population-based study as it requires clinical assessment from healthcare professionals.

2.3.5 Age

In term of age, there was a trend towards lower direct medical cost for older children and to a lesser extent for the total cost in India and Pakistan (Rheingans *et al.*, 2012). It was supported by Rochanathimoke *et al.* (2019) who observed a negative linear relationship between children's age group and the cost incurred due to acute diarrhoea. The older the children, the lower the direct medical cost and total cost. Nevertheless, in these two studies, the linear relationship was only applicable to children age less than five-year-olds since the study samples were among children in this age group.

Instead of focusing only on children under five years old, Sarker *et al.* (2018) examined the association between all age groups and the average household cost. The household cost was highest for the elderly aged more than 60 years old (USD107.10) compared to any other age groups. Nonetheless, if we were to compare the cost among

children, the cost for children aged more than five-year-olds was significantly higher than that of less than five-year-olds (USD65.90 vs USD43.83).

2.3.6 Inpatient care

Sarker *et al.* (2018) in their study revealed the cost incurred by households for inpatient care was significantly higher than outpatient care (USD83.70 vs USD22.52; p-value <0.001). This finding was parallel with a study in Bolivia where outpatient care became a protective factor (OR 0.16, 95% CI [0.07, 0.37]) of catastrophic cost among household compared to that of inpatient care (Burke *et al.*, 2014).

This difference was contributed by the expenditure such as cost for ward charges, transportation, food and lodging if patients were admitted. The indirect cost would also be higher for inpatient care since the days away from work will be longer. This was proven by the higher percentage of total cost contributed by indirect cost for inpatients (62.3%) compared to outpatients (40.7%) (Burke *et al.*, 2014).

2.3.7 Private versus public care

Burke *et al.* (2014) also revealed that families obtaining care from private hospitals had significantly higher incurred cost as compared to the families who received care at the public hospital (USD59 vs USD20).

2.4 Population-based survey

The National Health Morbidity Survey reported 43.3 % of the individuals affected with acute diarrhoeal disease sought treatment (Tee *et al.*, 2011). The main reasons for not seeking treatment were the illness was mild and respondents self-medicate at home. The study was in agreement with a population-based study in France which reported only 33.4% of respondents sought care for AGE (Van Cauteren *et al.*, 2012). Comparing with data from Sweden, it reported a significantly lower percentage (8.3-10.8%) of seeking treatment among children affected with AGE compared to the Malaysian and France data (Edelstein *et al.*, 2016). Episodes perceived as severe by the individuals or parents were more likely to seek care at GP and hospital.

Since most patients with AGE do not seek treatment, they are more likely to be in the community setting. Various methods can be applied to reach the general population who are affected by AGE, such as web-based survey, face-to-face interview, telephone and postal surveys. There are strengths and weaknesses of each method; hence the selection of the most appropriate method should be considered in tandem with the study objectives and requirements.

One of the methods to reach affected individuals regardless of their utilisation of healthcare services is via a web-based survey. The web-based survey is associated with limitations such as internet penetration, representativeness of study samples and low response rate. However, its usage undeniably can bring benefits and advantages to researchers, especially in this era of Industry 4.0. It is increasingly common in research as it offers wider distribution and faster data collection at lower cost with less error of data transfer (Maymone *et al.*, 2018).

In Japan, a web-based survey was used to measure the burden of paediatric AGE (Nakagomi *et al.*, 2013). An invitation e-mail was sent to women aged 20-44 years old whose names were listed in a Japanese database from an internet-based survey company. Those who were willing to participate would proceed with the questionnaire. The researchers opted to use this method to obtain a large number of samples nationwide in a short time. Besides, they would obtain more reliable data from the internet-literate respondents who were expected to be sufficiently intelligent to provide information (Nakagomi *et al.*, 2013).

Ecollan *et al.* (2020) conducted a web-based study to determine risk factors of AGE among the general population in France. Participants registered voluntarily online on a website as a part of syndromic surveillance in the general population. They were invited on a weekly basis to update on their symptoms during the winter season. Although the study is bound to be biased in respondents' representativeness; all ages, gender and level of education were represented in the survey.

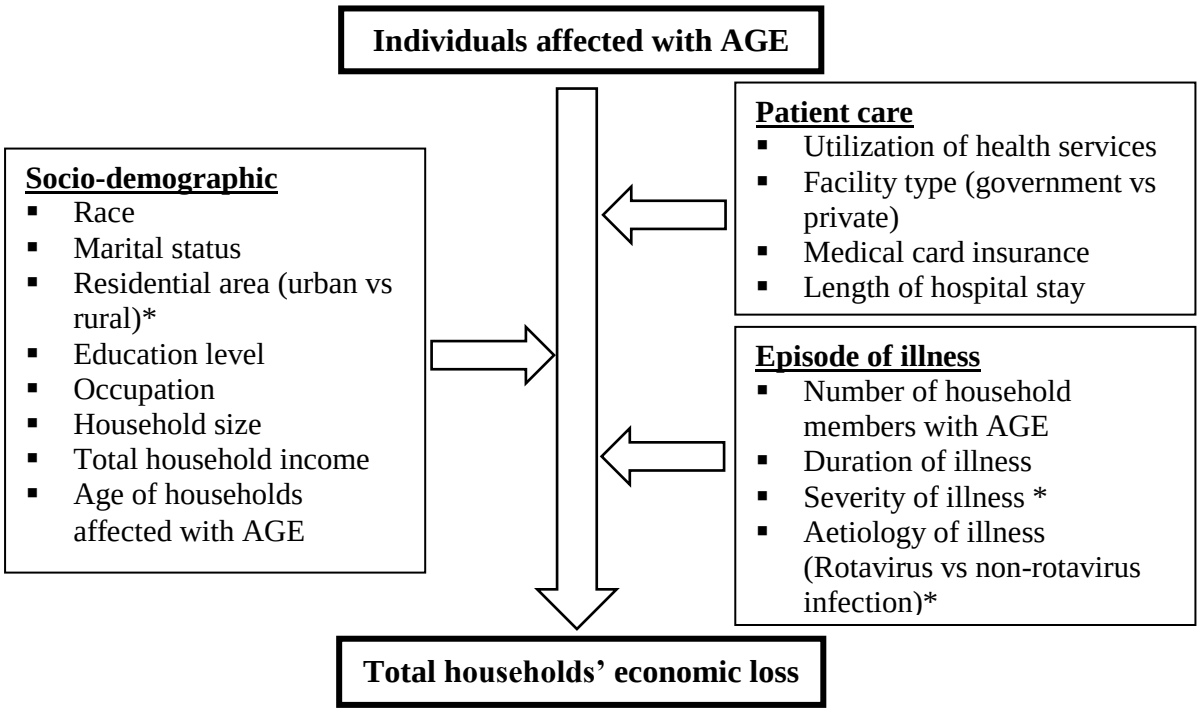
In Malaysia, the face-to-face approach was used in the National Morbidity Health Survey (NHMS) to determine the incidence of acute diarrhoea and health-seeking behaviour of those affected (Gurpreet *et al.*, 2011; Tee *et al.*, 2011). This approach produced high-quality data but incurred higher costs. On the contrary, Ho *et al.* (2009) conducted a study on the burden of AGE in Hong Kong using a population-based telephone survey. A random digit-dialling method was adopted based on residential telephone directories. A member of the households was chosen by the last birthday method. The same methodology was used by Adlam *et al.* (2011) to study AGE in New Zealand. The drawbacks of this telephone survey method were not every household has a telephone line and a possible tendency for another person claiming to

be the person with last birthday. Whereas in Sweden, randomly selected individuals were reached by postage based on the national residents' registry (Pilgaard *et al.*, 2015). Respondents were allowed to choose between completing a paper or web-based questionnaire (internet link attached to the letter) to increase the response rate.

In sum, many approaches were attempted in the previous studies to reach individuals with AGE in the general population. Every approach has its strengths and weaknesses. In the current study, despite its critiques, a web-based survey was chosen as the data collection method due to following reasons: (i) less costly with no additional expenses for interviewer wages, travel costs, telephone-, printing- and postage- charges; (ii) a large number of respondents can be obtained within a short period as there was no time lag for postal return time or interviewer travel time; (iii) better coverage as web-based is not limited by geographical barrier as compared to other methods and (iv) low risk for human processing errors during data transfer.

2.5 Conceptual framework

Based on the literature review, there were several factors which influenced households' total economic loss attributable to AGE. The identified factors were household income, residential area (urban vs rural), aetiology of illness (rotavirus vs non- rotavirus), severity of illness, age, inpatient care and facility types (government vs private care). However, factors such as severity of illness and aetiology of illness were not included in this study because these factors were difficult to assess without proper assessment from healthcare professionals and laboratory confirmation test. The residential area was also excluded due to difficulties in identifying the locality of participants' address. The outcome of interest is the total households' economic loss attributable to AGE. The total economic loss is the sum of direct healthcare cost, direct non-healthcare cost and indirect cost. Figure 2.1 illustrates the conceptual framework of the study.



Notes: Variables with symbol '*' were not studied

Figure 2.1: Conceptual framework of the study

CHAPTER 3

METHODOLOGY

3.1 Study design

This was a cross-sectional study.

3.2 Study period

This study was conducted between December 2019 and March 2020.

3.3 Study area

The study area was Malaysia.

3.4 Reference population

Individuals affected with AGE in Malaysia.

3.5 Source population

Individuals with self-reported AGE in Malaysia.

3.6 Sampling frame

Individuals with self-reported AGE in Malaysia who fulfilled the study criteria.

3.7 Subject criteria

The criteria of sample selection were as follows:

3.7.1 Inclusion criteria

i. A representative of a household whose member(s) had self-reported AGE that lasted <14 days within the past 12 months from the date of study participation, AND

ii. A representative of a household who was:

    1. Age more than 18 years old
    2. Malaysian who currently resided in Malaysia
    3. Able to understand Malay or English language

3.7.2 Exclusion criteria

i. A representative of a household who did not consent to the study.

ii. A representative of a household who consented but did not complete the web-survey.

3.8 Sample size determination

The sample size required to estimate the direct healthcare cost, direct non-healthcare costs and indirect cost (Specific Objective 1 and 2) was calculated using the sample size calculator for estimation of a single mean by Najib (2015). The formula is as follows:

$$n = \left(\frac{Z_{\alpha/2} * \sigma}{d} \right)^2$$

Where;
n = Calculated sample size
α = Type 1 error
σ = Standard deviation
d = Precision of estimates

Table 3.1: Sample size calculation for the direct healthcare, direct non-healthcare and indirect costs of AGE in Malaysia.

Cost	σ	**Precision**	α	**n**	**Corrected (n)**	**Literature**
Direct healthcare	93	10	5	333	370	(Loganathan, Lee *et al*. 2015)
Direct non-healthcare	19	5	5	56	63	(Loganathan, Lee *et al*. 2015)
Indirect	92	10	5	326	363	(Loganathan, Lee *et al*. 2015)

Note: σ, standard deviation (by literature); α, type 1 error; n, sample size calculated; corrected (n), number of sample required considering estimated 10% non-response rate.

The sample size calculation to determine the associated factors of total household economic loss should be calculated for each variable using local reference data. It would be unjust to apply international reference data since each country has a unique currency, healthcare system and health financing system. Since we did not explore on residential area and rotavirus infection, the only associated factor which was studied locally was households' income. Otherwise, local studies were limited to descriptive statistics or household catastrophic expenditure which was different from our research.

Hence an alternative approach was applied to determine the sample size. As suggested by Bujang *et al.* (2017), a larger sample size such as 300 or more is necessary for a non-experimental study. Whereas, according to Harrel (2001), the rule of thumb can be applied to calculate sample size for multiple linear regression analysis. The rule of thumb is ten times the number of independent variables. This current study explored 13 independent variables, therefore:

n=10×number of independent variables
n=10×13 independent variables in this study
n=130

The required sample size using the rule of thumb method was 130. However, this study adopted the largest calculated sample size which was 370 as shown in Table 3.1.

3.9 Sampling method and subject recruitment

In this study, convenience sampling was applied using a web-based survey.

3.10 Research tools and variables

The study researchers developed a costing proforma which was distributed using a paid web-based survey (Survey Monkey). Survey Monkey was used as it did not allow multiple submission using the same device. It was made available in English and Malay versions. The proforma contained a total of 26 questions encompassing socio-demographic details, patient care, episode of illness, direct cost and indirect cost. The