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Estimating the Economic Burden of Diarrhea in the United States Amongst the Privately
Insured In-Patient Population

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B. Phil., Miami University, 2009

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Environmental Health
2011

ABSTRACT

Estimating the Economic Burden of Diarrhea in the United States Amongst the Privately Insured In-Patient Population

By Alison R. Kernohan

Background:

While several studies have quantified the economic burden of diarrheal disease in the pediatric population, recent payment-based estimates for the U.S. population are rare and often limited to a particular diarrheal illness.

Objective:

This study used the MarketScan Commercial Claims and Encounters database to estimate the economic burden of hospitalizations due to diarrheal disease in the privately insured population between the ages of 0 and 64.

Methods:

The sample population was isolated from the larger database using ICD-9 codes of interest. Costs were then calculated for in-patient records hospitalized for diarrheal and delineated into two groups: those who had a diagnosis of interest coded as their primary diagnosis and those who had a diagnosis of interest listed as a secondary diagnosis. Additional analyses were conducted to determine the effect of immunocompromised status on costs, age, gender and region specific rates of hospitalization, seasonality and length of stay.

Results:

Between 2004 and 2008 the average cost per episode was \$7,926 for patients with a primary diagnosis of diarrhea (including \$7,266 in insurer payments and \$660 in out of pocket payments) and \$15,541 for patients with a secondary diagnosis of diarrhea (including \$14,680 in insurer payments and \$862 in out of pocket payments). Cost also varied significantly depending on whether the patient was immunocompromised or immunocompetent. Rates of diarrheal illness increased with age, were higher in females over males and were highest in the South as compared to other regions.

Discussion:

While diarrheal illness is predominately a self-limiting illness, people are still being hospitalized for treatment, significantly contributing to the domestic economic burden of diarrheal disease. Further research is needed to quantify the cost of those over the age of 64, and cases of diarrhea that are never hospitalized.

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ACKNOWLEDGEMENTS

This thesis would not have been possible without the guidance and the help of several individuals who in one way or another contributed and extended their valuable assistance in the preparation and completion of this project.

First and foremost, my utmost gratitude to Sarah Collier for her sincerity, expertise, flexibility and unwavering encouragement throughout this project; without her insightful comments and extensive understanding of the issues this thesis would have been a lot less meaningful, both statistically and personally.

Dr. Matt Strickland, for his patience, guidance and support as my academic and thesis advisor.

Dr. Paige Tolbert, for her involvement in this project over the past year and her support throughout my academic career.

Jonathon Yoder, for his willingness to go above and beyond the duties of a guest lecturer; without him this project would not have been possible.

My colleagues, family and friends for their unfailing understanding of the time and effort required to complete this project; your support through the past two years has been remarkable.

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I. INTRODUCTION

Diarrheal diseases are second only to acute respiratory diseases in worldwide occurrence (1) resulting in the loss of 62 million disability-adjusted life years (DALYs) annually (2). Although diarrheal disease morbidity and mortality are lower in the United States than in the developing world, a substantial burden still exists. Despite many improvements in sanitation and hygiene domestically, ten percent of pediatric hospitalizations (3) and approximately 3000 deaths are attributable to diarrheal illness each year (4).

Current Economic Estimates

Few studies have aimed to quantify the economic burden of diarrhea in the U.S., and those that have focused primarily on pediatric cases, most in response to rotavirus(5) (6) (7). While acute diarrhea is a common cause of hospital admission for children, (8) many adults also suffer from diarrhea, although the majority of the adult population costs are presumably due to the small number of high cost cases in the elderly population.

Enteric illnesses are known to be costly. Prior publications have suggested the annual economic burden of disease in the U.S. in the billion-to-trillion dollar range (9-11); estimates vary widely in scope and methodology. Some only measure for direct medical expenses, others account for indirect costs including work loss; many only examine a limited number of pathogens, though the majority of foodborne illness in the U.S. is estimated to be due to agents not yet identified (12). A more complete estimate would include direct healthcare costs for diarrheal disease from unidentified pathogens.

Some estimates exist for specific pathogens that cause diarrheal disease. For example, the Economics Research Bureau of the U.S. Department of Agriculture annual cost of illness for salmonellosis was approximately \$2.8 billion (13) and for *E. coli* O157 was \$405 million (in 2003 dollars) (14). However, to our knowledge, a recent, payment-based estimate of the overall cost of hospitalization for diarrhea in the U.S. population is not available. Given the estimated 38.4 million episodes of foodborne illness each year are caused by unknown organisms in the U.S., (12) an up-to-date estimate of the cost of hospitalization for diarrhea is needed to advance efforts to determine the burden and cost of preventable enteric illness in the U.S.

II. MATERIALS AND METHODS

In order to estimate the cost of domestic in-patient diarrheal cases, a large health insurance claims database was utilized as the primary sample source. Patients with a diagnosis of infectious diarrhea not further specified were identified from the larger sample, given non-infectious diarrhea cases are much less common (4). Descriptive statistics were used to estimate cost per hospitalization. Rates of hospitalization by age, gender geographic region, immune status and month were compared.

Data source

The MarketScan Commercial Claims and Encounters (CCAЕ) database was used as the only source of records for this study. The CCAЕ database is a large health insurance claims database that includes physician, hospital and pharmaceutical records for a convenience sample of people with employer-provided health insurance and their dependents. The database includes over 98.5 million unique patients since 1996 (15).

The database contains records from all 50 states for people aged 0-64 (persons aged 65 or older are eligible for Medicare; they are captured in a separate Medicare database, which was not included in these analyses).

Inclusion Criteria

The Commercial Claims and Encounters database lists up to 15 separate diagnostic codes for each case. The primary analysis sample was limited to patients who had one of the following ICD-9-CM codes of interest listed as their first (primary) diagnosis: infectious colitis, enteritis, and gastroenteritis (009.0), colitis, enteritis, and gastroenteritis of presumed infectious origin (009.1), infectious diarrhea (009.2), diarrhea of presumed infectious origin (009.3) and diarrhea not otherwise specified (787.91) (16). A patient with a secondary diagnosis of diarrhea was defined as a patient with an eligible diagnostic code in diagnoses 2-15.

Cost Calculation Methodology

The net insurer payment variable existing in the MarketScan CCAE database included all payments made by the insurance carrier for each patient (17). An out-of-pocket cost variable was made by summing pre-existing cost variables all paid by the patient, including their deductible, copayment and coinsurance. This out of pocket variable was then added to the pre-existing net insurer payment variable to create a total cost variable that reflected the sum of the total payments from the insurer and the insured person for each case.

To allow for comparisons between years, all costs were converted to 2008 dollars using the Medical Care Consumer Price Index calculated by the U.S. Department of Labor.

The newly converted variables were then used in a univariate analysis in SAS 9.2 (Cary, NC) to ascertain the mean cost per case for patients with a primary diagnosis of diarrhea over the five year period with a 95% confidence interval. The same methodology was used to calculate a second cost per hospitalization estimate for patients with a secondary diagnosis of diarrheal disease. A t-test was then conducted comparing the cost estimate means between the primary and secondary sample populations.

In addition, to assess trend over time, out-of-pocket, net insurer payment and the total payments were calculated for each year between 2004 and 2008. Yearly payment data variables were used to determine the Spearman correlation coefficient, testing for any cost trend over time.

Secondary Analyses

In addition to estimates of cost, secondary analyses included length of stay calculations, an examination of the rates of diarrhea within the sample population stratified by age, gender and geographic region as well as seasonality of admissions. A broader examination of immunocompromised patients who also possessed a secondary diarrheal diagnosis was also included.

Mean length of stay was calculated from admission and discharge dates from each patient record within the dataset. Using a univariate analysis within SAS 9.2, the interquartile range was also calculated. Mean length of stay was also calculated for patients with a primary or secondary diagnosis, and a t-test was used to assess the difference in length of stay between the two sample populations.

Rates of hospitalization by age, gender, and geographic region were calculate, using denominators that reflects total number of covered lives--anyone with a health plan/employer that reports info to MarketScan was included in the database regardless if they actually had a claim (from either an outpatient visit or hospitalization). An overall rate of hospitalization was also calculated individually for each of the study years to assess any trend over time.

To assess seasonality over the five year period, a month of admission variable, from the MarketScan admission date variable, was created for those with a primary or secondary diagnosis of diarrheal illness. A univariate analysis was run on the month of admission variable over the five year period to obtain the number of hospitalizations per month. These totals were then divided by the number of days within each month to estimate the average cases per day. These figures were then used to examine seasonality trends over the five year period as whole and compare any trends between the primary and secondary populations.

Using the sample population that included patients with a primary or secondary diagnosis of infectious diarrheal illness, immunocompromised patients were identified using the ICD-9 codes listed in the Prevention Quality Indicators Technical Specifications published by the Agency for Health Research and Quality (Appendix 1). Net insurance payments, out-of-pocket costs and totals were calculated for immunocompromised and immunocompetent patients as a group over the five year period. Cost per hospitalization,

with a 95% confidence interval was also calculated using a univariate analysis. These mean costs for each category were then compared using multiple t-tests among the groups.

III. RESULTS

There were 75,684 in-patient cases with at least one ICD-9 code of interest included in the MarketScan CCAE database. Of those, 7,912 cases had diarrheal illness as their primary diagnosis.

Economic Estimates

Average cost per episode was calculated (Table 1). Average cost per episode was \$7,926 for patients with a primary diagnosis of diarrhea (including \$7,266 in insurer payments and \$660 in out of pocket payments) and \$15,541 for patients with a secondary diagnosis of diarrhea (including \$14,680 in insurer payments and \$862 in out of pocket payments). Costs were significantly higher ($p < 0.0001$) for patients with a secondary diagnosis of diarrhea (on average \$7,616 higher (95% CI \$7,046-\$8,184)).

Table 1. Mean costs per case for privately insured in-patient diarrheal cases between 2004-2008

| <i>Diarrhea coded as:</i> | <i>Average length of stay in days</i> <i>IQR</i> | <i>Net insurer payment per case</i> <i>95% CI</i> | <i>Out of pocket cost per case</i> <i>95%CI</i> | <i>Total cost per case</i> <i>95% CI</i> |
|---------------------------|---|--|--|---|
| Primary Diagnosis | 3.17 2 | \$7,266 \$6,765 - \$7,766 | \$660 \$639 - \$681 | \$7,926 \$7,425 - \$8,247 |
| Secondary Diagnosis | 5.67 4 | \$14,680 \$14,416 - \$14,944 | \$862 \$830 - \$893 | \$15,541 \$15,272 - \$15,810 |

Length of stay analyses estimated the average length of stay over the five year period differed between those with a primary and secondary diagnosis (see Table 2). At the 5% level, there is sufficient evidence to suggest those primarily hospitalized for something other than had a longer length of stay than those with a hospitalized primarily for diarrhea ($t=36.39$, $p < 0.0001$). We are 95% confident that the true difference in length of stay is between 2.3 and 2.5 days, with a best estimate of 2.4 days.

Table 2. Length of Stay for a case of diarrhea within the United States between 2004-2008 (reported in days)

| <i>Diarrhea as:</i> | <i>Mean (IQR)</i> | <i>Median</i> | <i>Standard Deviation</i> |
|----------------------|-------------------|---------------|---------------------------|
| Primary Diagnosis | 3.17 (4-2) | 2 | 5.16 |
| Secondary Diagnosis | 5.57 (6-2) | 3 | 8.16 |
| Primary or Secondary | 5.32 (6-2) | 3 | 7.93 |

For net insurer payment, 2007 possessed the highest per case estimate, as well as the highest out-of pocket cost per case (see Table 3). However, the lowest net insurer payment per case estimate was in 2005, whereas the lowest out of pocket average cost per case was in 2006. Between the years 2004 to 2008, an estimated \$7,777 was spent on average for each in-patient record coded primarily for diarrheal disease within the MarketScan CCAE database.

Table 3. Cost per case estimates for in-patient records with a primary diagnosis of diarrhea by year

| | <i>Frequency</i> | <i>Net Insurer Payment Per Case</i> | <i>Out-of-Pocket Cost Per Case</i> | <i>Total Cost Per Case</i> |
|-------------------|------------------|---|--|----------------------------|
| 2004 | 1,083 | \$6,627 | \$645 | \$7,273 |
| 2005 | 1,138 | \$6,365 | \$641 | \$7,006 |
| 2006 | 1,236 | \$7,375 | \$620 | \$7,995 |
| 2007 | 1,998 | \$7,667 | \$696 | \$8,362 |
| 2008 | 2,457 | \$7,583 | \$666 | \$8,250 |
| 5 year Average | | \$7,124 | \$654 | \$7,777 |

When a Spearman correlation coefficient was calculated for each cost variable in relationship to year, a very weak positive correlation was observed between the net insurer payment ($r=0.04$, $p<0.0001$), out of pocket payment ($r=0.008$, $p < 0.0001$) and total payment ($r=0.04$, $p < 0.0001$) with year.

Population Demographics

The majority of patients with a primary diagnosis of diarrhea were adults, with 29 percent of the patients between the ages of 55 and 65. Hospitalization rates differed by age and ranged from 3.5 hospitalizations per 100,000 in 0-17 year olds to 17.8 hospitalizations per 100,000 in 55-64 year olds (Table 4). Females made up the majority of the primary sample population (62.1%) and had a higher rate of hospitalization for diarrheal disease than their male counterparts. Geographically, the largest number of cases was in the Southern region, which also had the highest rate of diarrheal disease, 9.7 hospitalizations per 100,000 (see Table 4).

Table 4. Specific rates of hospitalizations primarily from diarrheal disease within the privately insured MarketScan population between the years 2004-2008¹

| | <i>% of Cases</i> | <i>Rate per 100,000</i> | <i>Rate Ratio²</i> |
|----------------------------|-------------------|-------------------------|-------------------------------|
| Age (yrs) | | | |
| 0-17 | 10.6 | 3.5 | 1 |
| 18-34 | 18.5 | 6.7 | 1.9 |
| 35-44 | 17.4 | 9.0 | 2.6 |
| 45-54 | 24.5 | 11.9 | 3.4 |
| 55-64 | 29.0 | 17.8 | 5.1 |
| Sex | | | |
| Male | 37.9 | 6.9 | 1 |
| Female | 62.1 | 10.6 | 1.5 |
| Region | | | |
| Northeast ³ | 9.6 | 9.0 | 1.5 |
| North Central ⁴ | 26.4 | 9.2 | 1.5 |
| South ⁵ | 49.0 | 9.7 | 1.5 |
| West ⁶ | 14.3 | 6.2 | 1 |
| Unknown | 0.7 | 11.3 | 1.8 |

Overall, a linear trend over time in the rates of diarrheal disease was not observed (Table 5).

¹ Only accounts for hospitalized patients with diarrheal illness coded as their primary diagnosis

² Lowest rate listed was used as the reference group for age, sex and region rate comparisons

³ Northeast region includes: Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut, New York, New Jersey, Pennsylvania

⁴ North Central region includes: Ohio, Indiana, Illinois, Michigan, Wisconsin, Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas

⁵ Southern region includes: Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Tennessee, Alabama, Mississippi, Arkansas, Louisiana, Oklahoma, Texas

⁶ West region includes: Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada, Washington, Oregon, California, Alaska, Hawaii

Table 5. Rates of hospitalizations for diarrheal disease between the years 2004-2008

| Year | Percent | Rate per 100,000 |
|------|---------|------------------|
| 2004 | 13.7 | 9.8 |
| 2005 | 14.4 | 7.5 |
| 2006 | 15.6 | 8.6 |
| 2007 | 25.2 | 9.4 |
| 2008 | 31.1 | 8.7 |

Seasonality

When seasonality of admissions was examined, the total number of admissions each month ranged from an average of 227 admission records per day in February to an average of 194 admission records per day in December (see Figure 1). The number of admissions differed in those with a primary diagnosis, peaking in August with an average 25 cases admitted per day (see Figure 2).

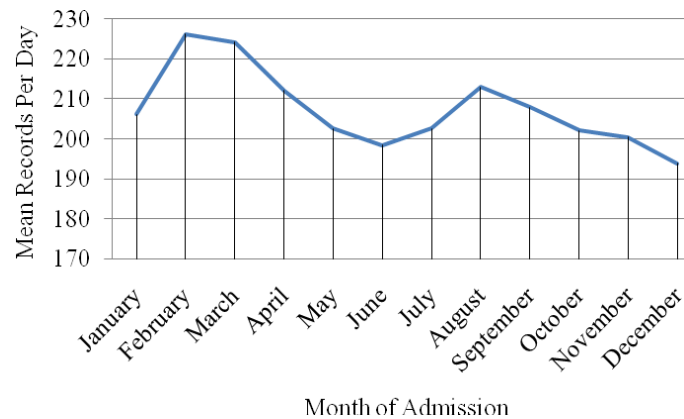


Figure 1. Mean hospital admissions involving any diagnosis of diarrhea per day by month of admission, 2004-2008.

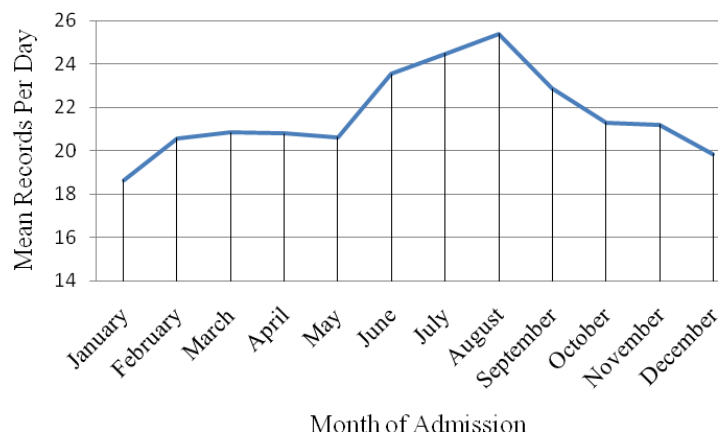


Figure 2. Mean hospital admissions involving a primary diagnosis of diarrhea per day by month of admission, 2004-2008.

In the population hospitalized primarily for diarrhea a different pattern was observed, with the average cases per day peaking in August and reaching the lowest number in January (Table 6).

Table 6. Seasonality of in-patient records of diarrheal disease by average cases per day for 2004-2008

| <i>Month</i> | <i>Diarrheal Diagnosis</i> | |
|--------------|----------------------------|------------------|
| | <i>Primary</i> | <i>Secondary</i> |
| January | 19 | 188 |
| February | 21 | 206 |
| March | 21 | 203 |
| April | 21 | 191 |
| May | 21 | 182 |
| June | 24 | 175 |
| July | 24 | 178 |
| August | 25 | 188 |
| September | 23 | 185 |
| October | 21 | 181 |
| November | 21 | 179 |
| December | 20 | 174 |

Immunocompromised Patients

Immunocompromised patients had a higher cost per case, with the highest costs in immunocompromised patients with a secondary diagnosis of diarrhea (see Table 7).

Table 7. Mean costs per case for hospitalized patients with a primary or secondary diagnosis of diarrhea by immune status , 2004-2008

| <i>Immune status</i> | <i>Frequency</i> | <i>Net insurer payment (95% CI)</i> | <i>Out of pocket cost (95%CI)</i> | <i>Total cost per case (95% CI)</i> |
|----------------------------|------------------|-------------------------------------|-----------------------------------|-------------------------------------|
| Primary diagnosis | | | | |
| Immunocompromised | 455 | \$18,668 \$10,746-\$26,592 | \$446 \$368-\$523 | \$19,114 \$11,189-\$27,040 |
| Immunocompetent | 7,457 | \$6,570 \$6,356-\$6,784 | \$673 \$652-\$694 | \$7,243 \$7,028-\$7,459 |
| Secondary diagnosis | | | | |
| Immunocompromised | 6,831 | \$32,773 \$31,060-\$34,487 | \$914 \$659-\$1169 | \$33,687 \$31,928 -\$35,447 |
| Immunocompetent | 60,941 | \$12,652 \$12,435-\$12,868 | \$855 \$836 -\$875 | \$13,507 \$13,288-\$13,727 |

On average, hospital stays for immunocompromised patients with a primary diagnosis of diarrhea cost \$11,871 more than immunocompetent patients hospitalized primarily for diarrhea (Table 8). Within the group of immunocompromised patients, hospital stays that included a secondary diagnosis of diarrhea were \$14,573 more costly than stays for patients with a primary diagnosis of diarrhea.

Table 8. Two-sample T-tests results comparing mean total cost for immunocompromised and immunocompetent patients with a primary or secondary diarrheal diagnosis between 2004-2008

| <i>Comparison Groups</i> | <i>Difference in Means</i> | <i>95% CI</i> | <i>t-value (p-value)</i> |
|---------------------------------------|----------------------------|---------------------|--------------------------|
| <i>Primary DX</i> | | | |
| Immunocompromised vs. Immunocompetent | \$11,871 | \$3,943 - \$19,800 | 2.94 (p=0.0034) |
| <i>Secondary DX</i> | | | |
| Immunocompromised vs. Immunocompetent | \$20,180 | \$18,407 - \$21,953 | 22.31 (p <0.0001) |
| <i>Immunocompromised</i> | | | |
| Secondary vs. Primary DX | \$14,573 | \$6,455 -\$22,691 | 3.53 (p=0.0005) |
| <i>Immunocompetent</i> | | | |
| Secondary vs. Primary DX | \$6,264.30 | \$5957 - \$6572 | 39.95 (p<.0001) |

IV. DISCUSSION

In the examination of hospitalizations between 2004-2008 total cost per case was higher in populations that possessed a secondary diagnosis of diarrhea. It is hypothesized that among the many factors influencing cost, longer length of stay and possessing an immunocompromised status contribute greatly to increases in the total cost figure.

Immunocompromised patients are more prone to infection, hospitalized more frequently, possess longer lengths of stay, and require more complex diagnosis and treatment than their immunocompetent counterparts (18) (19). This knowledge led us to think the cohort of immunocompromised patients within the secondary population was one of the main reasons for the significant cost increase over the primary population. However, the cost

figures generated in the univariate analysis suggest there was still a significant difference in cost, even when stratifying patients who are immunocompromised. The cost per case in the secondary population remained to be double the primary population. These results support the hypothesis that those hospitalized for another condition are more costly given that patients with diarrhea as one of many symptoms that may require complex testing and complicated treatment. For example, over ten percent of the study population had a primary diagnosis related to endocrine, nutritional or metabolic disorders many of which would include diarrhea in the symptomology, but standard diarrheal treatment would not be sufficient.

The population considered to be hospitalized primarily for diarrheal disease required limited diagnostic testing and lower cost methods of treatment, than those hospitalized for another illness, presumably in which diarrhea is one of other symptoms. It is assumed that this difference in diagnosis and treatment methodology, also accounts for the longer length of stay which is directly correlated with cost of hospitalization.

We recognize our \$7,243 per case estimate differs greatly from other figures in the literature, however, the \$2,255 per case estimate for those hospitalized after consultation with a physician was published in 1988, and when converted to 2008 dollars is still less than our calculated estimate by \$3,190 (20). To the author's knowledge all of these estimates use figures based upon the diagnosis and treatment of specific pathogens eg. salmonella and cryptosporidium.

Our estimate for the primary immunocompetent population is unique in the sense that it is largely representative of privately insured patients 0-64 years of age hospitalized for diarrheal disease, the majority of which remained undiagnosed. It is important to note that while this lower bound estimate was generated using data that is representative of the 52% of the U.S. general population (see Appendix B), our analysis only accounts for those who are hospitalized for the illness. Meaning the majority of those suffering from diarrheal illness are not accounted for in this estimate.

Uncomplicated diarrheal disease is usually self-limiting and the majority of those suffering from diarrheal disease never visit a physician (21-23). Of those who do seek medical attention, most are treated successfully without ever being hospitalized and often without identifying the specific pathogen (23-25). While we would hypothesize the costs in this population are much lower than those who require hospitalization, the number of patients is much greater. Previous studies have suggested there are an average of 211 million cases of gastroenteritis in the United States annually, of these 900,000 people are hospitalized and 6,000 die (26).

As a part of contextualizing our cost estimates within the existing literature, we examined the rates of hospitalization for diarrheal illness across the population, identified differences in age, gender and region specific rates and examined seasonality trends based upon average hospital admissions per month. While our analysis suggested that rates increase linearly as age increases, it does so within the constraints of predefined age brackets. The study population as a whole is skewed towards adults, and delineating a

difference between would require further analysis not included in this paper. It is possible that if the brackets were redistributed, a higher rate of hospitalizations for diarrheal illness would become apparent. It is also important to note the absence of the 65 and older population. We would expect the rates of hospitalization would increase even further in this population, but further analysis outside of this dataset would be needed to confirm such hypotheses.

Females made up the majority of the study population at 62 percent; however it is interesting to note the disparity between the rate of hospitalization between men and women for a primary diagnosis of diarrhea. We expect that there are numerous factors that have lead to this divergence. Main hypotheses include irritable bowel syndrome, a condition predominant in females (27) may be a cause of hospitalization primarily for diarrhea, the varying patterns in health care seeking behavior between males and females and the higher rates of morbidity in women within the U.S., however diarrheal disease hospitalization rates have never been documented domestically. International studies, including one from Bangladesh have documented higher hospitalization rates in females over males especially as age increases (28).

The results from the rate calculations based upon geographic region suggesting a greater risk of diarrheal illness in the South over other regions of the U.S.. This could be due to a number of factors including differences in diagnosis techniques, health care seeking behavior or seasonality of different pathogens. While the specific reasoning for this

trend is still unclear, the findings are consistent with those in a paper that examined infant mortality related to diarrheal disease with a similar methodology (29).

The lack of a linear trend in the seasonality analysis was to be expected given our hypothesis that in using diarrheal disease coded as the primary diagnosis we are actually capturing different undiagnosed food and water borne diseases. Due to the difference in seasonality peaks between these diseases, it makes sense that from month to month we would not see drastic changes, unless we knew which specific diseases they were. However, the lack of the trend may be due to the seasonal differences in the pathogens responsible for the majority of the diarrheal cases. Norovirus and rotavirus are most common in the winter (30, 31) while foodborne and swimming-associated enteric illness is more frequent in the summer. When the primary population was separated from the total study population and seasonality was graphed, hospitalizations increased, further suggesting our primary population is suffering from food and/or water borne illness.

Limitations

Although the MarketScan commercial claims and encounters database is very large, it is based on a convenience sample of employers and health plans willing to share billing data with MarketScan. While the data may be generalizable to the privately insured U.S. population when weights are applied, our cost estimates may not be nationally representative. MarketScan database receives the majority of its sample data from large employers and only include those who are commercially insured. Per case cost estimates for persons eligible for Medicare, Medicaid, or other health plans may differ.

Given the limits of our population we would suggest that this per case estimate is a lower bound figure for undiagnosed diarrhea in the United States, as it does not include any outpatient cases, or those patients who are above the age of 64, a population that is known for higher rates of diarrhea.

This research was also highly dependent on ICD-9 codes for sample selection and analysis. It functions under the assumption that the majority of the cases within the sample population were coded correctly and were in fact hospitalized for diarrhea. A factor that we aimed to control by separating the total population based upon where the ICD-9 code of interest fell within the billing record.

V. CONCLUSION

While our economic estimate is limited in scope, it suggests a lower bound number for the cost of hospitalization within the U.S. for diarrhea not otherwise specified. In beginning to quantify costs, we learned whether diarrhea was coded as primary or secondary, the patient's immunocompromised status and subsequent longer length of stay within the hospital are all factors that can increase the cost of hospitalization for diarrhea. Further research is needed to quantify these and other factors in the out-patient population.

WORKS CITED

1. DuPont HL. The Diarrhea Burden in Industrialized Countries. *Infectious Diseases in Clinical Practice* 1995;4(5):386-388.
2. World Health Organization. *World Health Report 2004: Changing History*. In. Geneva: WHO; 2004.
3. Glass RI, Lew, J.F., Gangarosa, R.E., LeBaron, C.W., Ho, M. Estimates of morbidity and mortality rates for diarrheal diseases in American children. *J Pediatr* 1991;118:27-33.
4. Nathwani D, Davey, Peter G. The Socioeconomic Impact and Management of Adult Diarrhea in Primary Care: Is There Variation? A Personal Viewpoint. *Infectious Diseases in Clinical Practice* 1995;4(5):380-386.
5. Cortes JE, Curns AT, Tate JE, Parashar UD. Trends in healthcare utilization for diarrhea and rotavirus disease in privately insured US children <5 years of age, 2001-2006. *Pediatr Infect Dis J* 2009;28(10):874-8.
6. Pont SJ, Grijalva CG, Griffin MR, Scott TA, Cooper WO. National rates of diarrhea-associated ambulatory visits in children. *J Pediatr* 2009;155(1):56-61.
7. Zimmerman CM, Bresee JS, Parashar UD, Riggs TL, Holman RC, Glass RI. Cost of diarrhea-associated hospitalizations and outpatient visits in an insured population of young children in the United States. *Pediatr Infect Dis J* 2001;20(1):14-9.
8. Guerrant RL, Hughes, J.M, Lima, N.L., Crane, J. Diarrhea in developed and developing countries: magnitude, special settings and etiologies. *Rev Infect Dis* 1990;12(1 Suppl):41S-50S.
9. Roberts T, Murrell KD, Marks S. Economic losses caused by foodborne parasitic diseases. *Parasitol Today* 1994;10(11):419-23.
10. Scharff RL, McDowell J, Medeiros L. Economic cost of foodborne illness in Ohio. *J Food Prot* 2009;72(1):128-36.
11. Widdowson MA MM, Zhang X, Bresee JS, Parashar UD, Glass RI. Cost-effectiveness and potential impact of rotavirus vaccination in the United States. *Pediatrics* 2007;119(4):684-97.
12. Scallan E GP, Angulo FJ, Tauxe RV, Hoekstra RM. Foodborne illness acquired in the United States—unspecified agents. In: *Emerg Infect Dis*. Jan 2011 ed; 2011.
13. Bishwa Adhikari FA, and Martin Meltzer. Economic Burden of Salmonella Infections in the United States. In; 2004.
14. Frenzen PD DA, Angulo FJ. . Economic cost of illness due to Escherichia coli O157 infections in the United States. *J Food Prot* 2005;68(12):2623-30.
15. Hansen LaC, Stella. *Health Research Data for the Real World: The MarketScan Databases*. 2009.
16. National Center for Health Statistics and Centers for Medicare & Medicaid Services. *The International Classification of Diseases, 9th Revision, Clinical Modification*. In; 2009.
17. Reuters T. *Commerical Claims and Encounters Data Dictionary*. In; 2009.
18. Thom KF, Graeme. Gastrointestinal infections in immunocompromised hosts. *Current Opinion in Gastroenterology* 2006;22(1):18–23.
19. Aranda-Michel J, Giannella RA. Acute diarrhea: a practical review. *The American Journal of Medicine* 1999;106(6):670-676.

20. Garthwright W.E. Archer DLK, J.E. . Estimates of incidence and costs of intestinal infectious diseases in the United States. *Public Health Rep* 1988;103:107-1125.
21. H. Herikstad SY, T.J. Vangilder, D. Vugia, J. Hadler, P. Blake, V. Deneen, B. Shiferaw, F.J. Angulo and Foodnet Working Group,. A population-based estimate of the burden of diarrhoeal illness in the United States : FoodNet, 1996±. *Epidemiol Infect* 2002;129:9-17.
22. Imhoff B MD, Shiferaw B, Hawkins M, Vugia D, Lance-Parker S, Hadler J, Medus C, Kennedy M, Moore MR, Van Gilder T. Burden of self-reported acute diarrheal illness in FoodNet surveillance areas, 1998-1999. *Clin Infect Dis* 2004;38(Suppl 3):19-26
23. T. F. Jones MBM, E.S. Callan, P.D. Frenzen, A.B. Cronquist, S. Thomas and F. J. Angulo. A population-based estimate of the substantial burden of diarrhoeal disease in the United States; FoodNet, 1996–2003. *Epidemiol Infect* 2007;135:293-301.
24. Voetsch AC AF, Rabatsky-Ehr T, Shallow S, Cassidy M, Thomas SM, Swanson E, Zansky SM, Hawkins MA, Jones TF, Shillam PJ, Van Gilder TJ, Wells JG, Griffin PM; Emerging Infections Program FoodNet Working Group. Laboratory practices for stool-specimen culture for bacterial pathogens, including *Escherichia coli* O157:H7, in the FoodNet sites, 1995-2000. *Clin Infect Dis* 2004;38(Suppl 3):190-7.
25. Tauxe RV CM, Blaser MJ. . *Epidemiology of diarrheal diseases in developed countries*. New York: Raven Press; 1995.
26. Mead PS, Slutsker L, Griffin PM, Tauxe RV. Food-related illness and death in the united states reply to dr. hedberg. *Emerg Infect Dis* 1999;5(6):841-2.
27. Jeremy H, Pokkunuri VB, Pimentel M. M1238 The Severity of Diarrhea and Constipation Are Important in Examining Gender Differences in IBS. *Gastroenterology* 2009;136(5, Supplement 1):A-379.
28. Chen L. Control of diarrheal disease morbidity and mortality: some strategic issues. *American Journal of Clinical Nutrition* 1978;31:2284-2291.
29. Kilgore PE, Holman RC, Clarke MJ, Glass RI. Trends of Diarrheal Disease—Associated Mortality in US Children, 1968 Through 1991. *JAMA: The Journal of the American Medical Association* 1995;274(14):1143-1148.
30. T. Miyoshi KU, M. Matsuo, Y. Ikeda, H. Yoshida, H. Sibata, F. Fujii, T. Tanaka,. Characteristics of Norovirus Outbreaks during a Non-Epidemic Season. *Jpn. J. Infect. Dis.* 2006;59.
31. U. Parashar CG, J. Bresee, R. Glass, . Rotavirus and Severe Childhood Diarrhea. *Emerg Infect Dis* 2006;12(2).

APPENDIX A:
ICD-9 CODES USED TO IDENTIFY IMMUNOCOMPROMISED PATIENTS

042 Human Immunodeficiency Virus Disease
1363 Pneumocystosis
23873 Hi Grde Myelodys Syn Les
23876 Myelofi W Myelo Metaplas
260 Kwashiorkor
261 Nutritional Marasmus
262 Oth Severe Malnutrition
27900 Hypogammaglobulinem Nos
27901 Selective Iga Immunodef
27902 Selective Igm Immunodef
27903 Selective Ig Defic Nec
27904 Cong Hypogammaglobulinem
27905 Immunodeficient W Hyper-Igm
27906 Common Variabl Immunodef
27909 Humoral Immunity Def Nec
27910 Immundef T-Cell Def Nos
27911 Digeorges Syndrome
27912 Wiskott-Aldrich Syndrome
27913 Nezelofs Syndrome
27919 Defic Cell Immunity Nos
2792 Combined Immunity Deficiency
2793 Unspecified Immunity Deficiency
2794 Autoimmune Disease, Not Elsewhere Classified
2798 Other Specified Disorders Involving The Immune Mechanism
2799 Unspecified Disorder Of Immune Mechanism
28409 Const Aplastic Anemia Nec
2841 Pancytopenia
2880 Agranulocytosis
28800 Neutropenia Nos
28801 Congenital Neutropenia
28802 Cyclic Neutropenia
28803 Drug Induced Neutropenia
28809 Neutropenia Nec
2881 Function Dis Neutrophils
2882 Genetic Anomaly Leukocyt
2884 Hemophagocytic Syndromes
28850 Leukocytopenia Nos
28851 Lymphocytopenia
28859 Decreased Wbc Count Nec
28953 Neutropenic Splenomegaly
28983 Myelofibrosis
40301 Mal Hyp Kidney W Chr Kid
40311 Ben Hyp Kidney W Chr Kid

40391 Hyp Kidney Nos W Chr Kid
40402 Mal Hy Hrt/Kid W Chr Kid
40403 Mal Hyp Hrt/Kid W Hf/Kid
40412 Ben Hyp Ht/Kid W Chr Kid
40413 Ben Hyp Ht/Kid W Hf/Kid
40492 Hyp Ht/Kid Nos W Chr Kid
40493 Hyp Hrt/Kid Nos W Hf/Kid
5793 Intest Postop Nonabsorb
585 Chronic Renal Failure
5855 Chron Kidney Dis Stage V
5856 End Stage Renal Disease
9968 Complications Of Transplanted Organ
99680 Comp Organ Transplnt Nos
99681 Compl Kidney Transplant
99682 Compl Liver Transplant
99683 Compl Heart Transplant
99684 Compl Lung Transplant
99685 Compl Marrow Transplant
99686 Compl Pancreas Transplnt
99687 Comp Intestine Transplnt
99689 Comp Oth Organ Transplnt
V420 Kidney Replaced By Transplant
V421 Heart Replaced By Transplant
V426 Lung Replaced By Transplant
V427 Liver Replaced By Transplant
V428 Other Specified Organ Or Tissue
V4281 Bone Marrow Specified By Transplant
V4282 Peripheral Stem Cells Replaced By Transplant
V4283 Pancreas Replaced By Transplant
V4284 Intestines Replace By Transplant
V4289 Other Replaced By Transplant
V451 Renal Dialysis Status
V560 Renal Dialysis Encounter
V561 Ft/Adj Xtrcorp Dial Cath
V562 Fit/Adj Perit Dial Cath

APPENDIX B:
HEALTH INSURANCE STATUS IN THE UNITED STATES

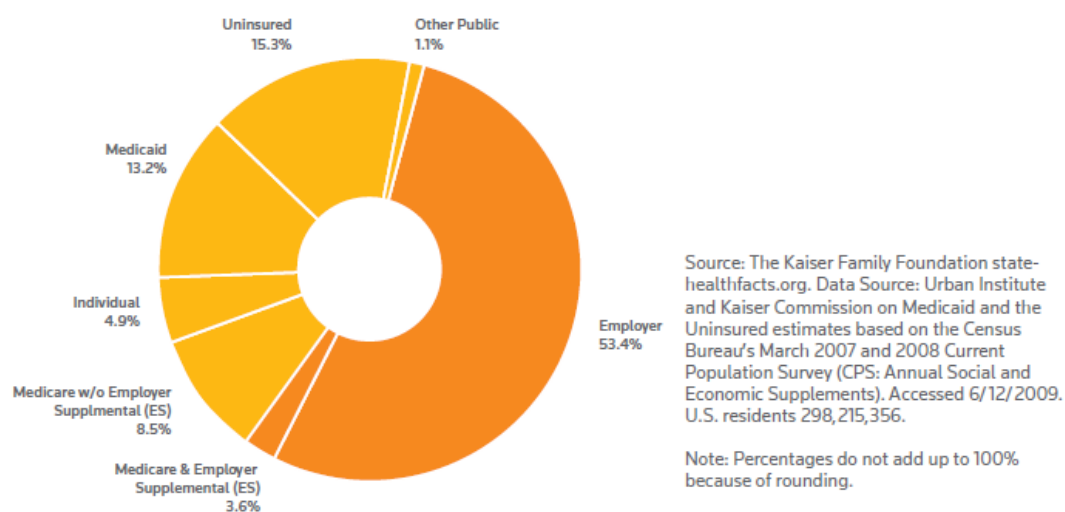


Figure A1. Health insurance status for the United States population

The MarketScan database accounts for approximately twelve percent of the 53.4 percent of people that use employer based insurance. Weights are available to make results applicable to the larger privately insured population, however they were not used in this thesis due to the inconsistencies of the weights.

APPENDIX C: PRELIMINARY RESEARCH

The preceding manuscript is a product of a project originally suggested by Sarah Collier in the National Center for Zoonotic, Vector-borne and Enteric Diseases of the Centers for Disease Control and Prevention (CDC). The following is a collection of analyses that were necessary for the final manuscript to be produced, but were not incorporated into the draft.

Background

The CDC along with the World Health Organization and the World Bank have recently become invested in determining the contribution of food and water borne illness to the over disease burden both in the United States and internationally. In the past year the National Center for Zoonotic, Vector-borne and Enteric Diseases at CDC began calculating the economic burden estimates of a number of water-related diseases. Given most food and water borne illness is self-limiting and for those who do make it into the hospital large cost of diagnostics tests and the effective, albeit limited, treatment options result in only a fraction of the food and water borne diseases being attributed to a specific pathogen. This project was designed to quantify this undiagnosed portion of food and water borne disease as a means for comparison to the more pathogen specific cost estimates.

Methods and Results

The sample for this project, including the manuscript, was pulled from the larger MarketScan database, to which CDC is a subscriber. After reviewing the literature it was

decided that diarrheal illness not otherwise specified would be an appropriate indicator for those who had a case of diarrheal illness, which we assume food and water borne pathogens are a likely cause. Using SAS 9.2 ICD-9 codes related to non-infectious diarrhea (009.0-009.3 and 787.91) were used to separate in-patients of interest. All of those who at least one ICD-9 code of interest between the years 2004 and 2008, were included in our initial analyses.

Because the MarketScan database provides a large and statistically powerful sample size, it was first important to validate the use of the ICD-9 codes chosen, to ensure the majority of the population did in fact have some sort of gastrointestinal illness. To do this I used the major diagnostic category (MDC) variable that is unique to MarketScan and delineates the primary reason a patient was hospitalized into one of 15 categories. The result of this analysis showed that even though only 51 percent of the total study population had a MDC related to the digestive system, it was still in the vast majority when compared to any other MDC (see Table A1).

Table A1. Major Diagnostic Category for the sample population

| Major Diagnostic Category | Frequency | Percent |
|--|-----------|---------|
| Digestive System | 39160 | 51.74 |
| Endocrine, Nutritional and Metabolic Disorders | 8153 | 10.77 |
| Respiratory System | 3878 | 5.12 |
| Kidney and Urinary Tract | 3367 | 4.45 |
| Infectious and Parasitic Diseases | 3149 | 4.16 |
| Circulatory System | 2922 | 3.86 |
| Heptobiliary System and Pancreas | 2805 | 3.71 |
| Nervous System | 1745 | 2.31 |
| Blood, Blood Forming Organs, Immunological Disorders | 1483 | 1.96 |
| Myeloproliferative Diseases and Disorders | 1265 | 1.67 |
| Musculoskeletal System and Connective Tissue | 1200 | 1.59 |
| Pregnancy, Childbirth and Puerperium | 1023 | 1.35 |

| | | |
|---|-----|------|
| Mental Diseases and Disorders | 984 | 1.3 |
| Skin, Subcutaneous Tissue and Breast | 886 | 1.17 |
| Female Reproductive System | 707 | 0.93 |
| Injuries, Poisonings and Toxic Effects of Drugs | 600 | 0.79 |
| Ear, Nose, Mouth and Throat | 557 | 0.74 |
| Factors Influencing Health Status and Other Contacts with Health Services | 517 | 0.68 |
| Human Immunodeficiency Virus Infections | 459 | 0.61 |
| Alcohol/Drug Use | 404 | 0.53 |
| Newborns and other Neonates | 257 | 0.34 |
| Male Reproductive System | 94 | 0.12 |
| Eye | 37 | 0.05 |
| Multiple Significant Trauma | 23 | 0.03 |
| Burns | 8 | 0.01 |
| Missing | 1 | 0 |

In addition to aiding in the validation of our sample selection methods, this analysis also suggests that in about half of our sample, patients are hospitalized for something other than diarrhea, and the reasoning is extremely variable patient to patient. This is when we first had the inclination of separating out the primary diagnosis variable (DX1) from all the other secondary diagnosis variables (DX2-DX15). However, costs were initially calculated for the group as whole using all cost variables available in the MarketScan database. This included the net insurer payment (see Table A2), deductible (see Table A3), copayments (see Table A4), coinsurance (see Table A5), certificate of benefits (see Table A6), and gross payments (see Table A7).

| Year | Median | Mean | Sum |
|------|------------|-------------|------------------|
| 2004 | \$4,528.12 | \$9,844.27 | \$87,239,910.12 |
| 2005 | \$4,828.53 | \$10,195.74 | \$94,891,774.47 |
| 2006 | \$5,606.93 | \$12,018.39 | \$104,956,579.21 |
| 2007 | \$6,076.84 | \$12,532.09 | \$232,407,633.80 |
| 2008 | \$6,800.56 | \$13,604.10 | \$331,545,473.60 |

Table A3. Deductible Payments from Patient

| Year | Median | Mean | Sum |
|------|--------|----------|----------------|
| 2004 | \$0.00 | \$177.21 | \$1,570,464.89 |
| 2005 | \$0.00 | \$92.24 | \$858,433.64 |
| 2006 | \$0.00 | \$126.44 | \$1,104,202.96 |
| 2007 | \$0.00 | \$166.19 | \$3,082,008.44 |
| 2008 | \$0.00 | \$163.66 | \$3,988,517.29 |

Table A4: Copayments made by the patient

| Year | Median | Mean | Sum |
|------|--------|----------|----------------|
| 2004 | \$0.00 | \$158.14 | \$1,401,437.08 |
| 2005 | \$0.00 | \$157.42 | \$1,465,080.33 |
| 2006 | \$0.00 | \$75.67 | \$660,777.72 |
| 2007 | \$0.00 | \$65.23 | \$1,209,757.80 |
| 2008 | \$0.00 | \$68.68 | \$1,673,783.53 |

Table A5. Coinsurance Payments made by the patient

| Year | Median | Mean | Sum |
|------|----------|----------|-----------------|
| 2004 | \$0.00 | \$427.15 | \$3,785,454.58 |
| 2005 | \$0.00 | \$417.70 | \$3,887,485.20 |
| 2006 | \$71.95 | \$592.83 | \$5,177,169.89 |
| 2007 | \$196.14 | \$544.76 | \$10,102,544.70 |
| 2008 | \$84.96 | \$537.96 | \$13,110,727.88 |

Table A6. Certificate of Benefits and other savings to the insurer

| Year | Median | Mean | Sum |
|------|--------|----------|----------------|
| 2004 | \$0.00 | \$385.63 | \$3,417,469.52 |
| 2005 | \$0.00 | \$314.71 | \$2,928,975.33 |
| 2006 | \$0.00 | \$405.45 | \$3,540,789.41 |
| 2007 | \$0.00 | \$353.61 | \$6,557,800.17 |
| 2008 | \$0.00 | \$355.17 | \$8,655,948.26 |

Table A7. Total gross cost

| Year | Median | Mean | Sum |
|--------|------------|-------------|------------------|
| 2004 | \$5,342.51 | \$11,337.72 | \$100,474,883.04 |
| 2005 | \$5,648.39 | \$11,403.11 | \$106,128,700.84 |
| 2006 | \$6,383.84 | \$13,418.86 | \$117,186,842.75 |
| 2007 | \$6,923.32 | \$13,756.37 | \$255,111,831.81 |
| 2008 | \$7,704.53 | \$14,943.40 | \$364,185,665.18 |
| Av All | | | \$188,617,584.72 |

After total cost estimates were figured in 2008 dollars, it was then determined that the costs should only include net payment from the insurer and the out of pocket estimates. In addition, the sample was then separated by primary and secondary diagnostic coding. Further analysis was then incorporated into the manuscript.