Journal of Food Protection, Vol. 68, No. 12, 2005, Pages 2623–2630

Economic Cost of Illness Due to *Escherichia coli* O157 Infections in the United States

PAUL D. FRENZEN,[1]* ALISON DRAKE,[2]† FREDERICK J. ANGULO,[2] AND THE EMERGING INFECTIONS PROGRAM FOODNET WORKING GROUP[2]

[1]*Economic Research Service, U.S. Department of Agriculture, 1800 M Street N.W., Washington, D.C. 20036-5831; and* [2]*Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road N.E., Atlanta, Georgia 30333, USA*

MS 05-277: Received 31 May 2005/Accepted 23 August 2005

ABSTRACT

The Centers for Disease Control and Prevention (CDC) has estimated that Shiga toxin–producing *Escherichia coli* O157 (O157 STEC) infections cause 73,000 illnesses annually in the United States, resulting in more than 2,000 hospitalizations and 60 deaths. In this study, the economic cost of illness due to O157 STEC infections transmitted by food or other means was estimated based on the CDC estimate of annual cases and newly available data from the Foodborne Diseases Active Surveillance Network (FoodNet) of the CDC Emerging Infections Program. The annual cost of illness due to O157 STEC was $405 million (in 2003 dollars), including $370 million for premature deaths, $30 million for medical care, and $5 million in lost productivity. The average cost per case varied greatly by severity of illness, ranging from $26 for an individual who did not obtain medical care to $6.2 million for a patient who died from hemolytic uremic syndrome. The high cost of illness due to O157 STEC infections suggests that additional efforts to control this pathogen might be warranted.

Shiga toxin–producing *Escherichia coli* O157 (O157 STEC) is an important cause of foodborne illness in the United States *(28)*. Cattle are a major reservoir for this pathogen *(24)*. Humans usually become infected by eating beef or other foods contaminated by O157 STEC *(15, 20, 29)*. Infections also have been caused by drinking or swimming in contaminated water, person-to-person transmission, contact with infected farm animals, and the apparent ingestion of airborne contaminated sawdust *(20, 29, 41)*. Individuals with symptomatic O157 STEC infections usually develop diarrhea, which is often bloody. Some infections result in hemolytic uremic syndrome (HUS), a systemic complication involving acute kidney failure. HUS may result in death or end-stage renal disease (ESRD), a serious chronic condition that reduces life expectancy *(40)*.

O157 STEC infections impose substantial economic costs on society. The Economic Research Service (ERS) of the U.S. Department of Agriculture estimated that the annual cost of illness due to O157 STEC transmitted by food or other means ranged from $0.4 to $2.7 billion in the United States in 1995 *(9, 10)*. The ERS cost estimate was based on the assumption that O157 STEC causes 10,000 to 20,000 illnesses annually, resulting in 1,800 to 3,600 hospitalizations and 220 to 541 deaths *(9, 10)*. The Centers for Disease Control and Prevention (CDC) subsequently estimated that O157 STEC caused 73,480 illnesses in 1997, resulting in 2,168 hospitalizations and 61 deaths *(28)*. In the present study, an updated estimate of the economic cost of illness due to O157 STEC from all sources of infection was developed based on the CDC estimate of the annual health burden plus newly available data from the Foodborne Diseases Active Surveillance Network (FoodNet) of the CDC Emerging Infections Program.

MATERIALS AND METHODS

FoodNet data. Information about laboratory-diagnosed O157 STEC infections was obtained from FoodNet surveillance data. FoodNet conducts active surveillance of clinical laboratories for laboratory-diagnosed O157 STEC infections in participating sites *(19)*. FoodNet also conducts active surveillance of pediatric nephrologists for pediatric HUS cases and passive surveillance for adult HUS cases *(19)*. The area under surveillance has expanded over time and covered all or part of nine states and 13% of the U.S. population in 2002 *(19)*. The O157 STEC and HUS surveillance data for 1997 through 2002 were linked to identify patients who developed HUS. The linked data included 3,201 laboratory-diagnosed patients, of whom 1,194 (37.3%) were hospitalized, 189 (5.9%) developed HUS, and 29 (0.9%) died. The linked data report patient age and other characteristics but do not indicate whether HUS patients developed ESRD.

Information about the effect of O157 STEC infections on health and productivity was obtained from two special FoodNet studies. Data on O157 STEC infections that were laboratory diagnosed were obtained from the 1999–2000 FoodNet *E. coli* O157 case-control study *(26)*. For the case-control study, FoodNet staff conducted telephone interviews with 481 of the 585 patients (82.2%) with a laboratory-diagnosed O157 STEC infection, including 28 patients who developed HUS, identified during clinical laboratory surveillance from February 1999 through April 2000 in seven participating FoodNet sites. The characteristics of O157 STEC infections that were not laboratory confirmed were estimated using data from the 2002–2003 FoodNet Population Survey

* Author for correspondence. Tel: 202-694-5351; Fax: 202-694-5688; E-mail: pfrenzen@ers.usda.gov.

† Present address: Department of Epidemiology, School of Public Health and Community Medicine, University of Washington, Box 357236, Seattle, WA 98195-7236, USA.

TABLE 1. *Classification of CDC estimate of annual O157 STEC cases by severity category, United States*[a]

Severity category	Estimated no. of annual O157 STEC cases	% of total annual O157 STEC cases	Data sources
1. Did not visit a physician: person not hospitalized and survived	57,656	78.46	FoodNet Population Survey respondents with an acute diarrheal episode who did not visit a physician
2. Visited a physician: patient not hospitalized and survived	13,656	18.58	See categories 2a and 2b
a. Not laboratory diagnosed	9,641	13.12	FoodNet Population Survey respondents with an acute diarrhea episode who visited a physician but were not hospitalized and did not provide a stool specimen
b. Laboratory diagnosed	4,015	5.46	Nonhospitalized FoodNet *E. coli* O157 case-control study respondents, FoodNet surveillance data
3. Hospitalized, did not develop HUS: patient survived	1,797	2.45	Hospitalized FoodNet *E. coli* O157 case-control study respondents who did not develop HUS and survived, FoodNet surveillance data
4. Hospitalized, developed HUS but not ESRD: patient survived	300	0.41	Hospitalized FoodNet *E. coli* O157 case-control study respondents who developed HUS and survived, FoodNet surveillance data
5. Hospitalized, developed HUS and ESRD: patient survived	10	0.01	Estimates for category 4, HUS patient studies *(13, 16, 21)*, data on U.S. ESRD population *(37)*
6. Patient died, did not develop HUS	23	0.03	Estimates for category 3, FoodNet surveillance data
7. Patient died, developed HUS	38	0.05	Estimates for category 4, FoodNet surveillance data
Total	73,480	100.00	

[a] CDC, Centers for Disease Control and Prevention; STEC, Shiga toxin–producing *E. coli* O157; HUS, hemolytic uremic syndrome; ESRD, end-stage renal disease.

(32), in the absence of other sources of information about undiagnosed cases. For the Population Survey, a survey contractor conducted telephone interviews of 16,435 residents of the FoodNet surveillance sites from March 2002 through February 2003, using Behavioral Risk Factor Surveillance System sampling methodology *(35)*. The survey identified 842 persons who had an acute diarrhea episode during the previous month but did not obtain medical care for their illness or else visited a physician but were not hospitalized and did not provide a stool specimen for clinical laboratory tests *(25)*. These persons were assumed to be representative of O157 STEC cases that were not laboratory confirmed or hospitalized. The Population Survey response rate was 27.4% based on the formula recommended by the Council of American Survey Research Organization *(32)*, exceeding the average response rate of 12% for commercial telephone surveys employing similar random-digit dialing methods *(36)*. The survey results were weighted to represent the population of the FoodNet sites classified by age and sex.

The FoodNet case-control study and Population Survey both asked detailed questions about the respondent's illness, which was the O157 STEC infection for the case-control study and the acute diarrhea episode for the Population Survey. The topics investigated included the duration and symptoms of illness, physician and emergency department visits, outpatient medication use, hospital stays, and time missed from work by employed persons. In both studies, a proxy interview was conducted with a parent or guardian if the designated respondent was a child <12 years of age.

Classification of O157 STEC cases by severity. The FoodNet data were used to expand the CDC estimate of annual O157 STEC cases, hospitalizations, and deaths into seven severity categories to better describe the outcome of O157 STEC infections (Table 1). Nonhospitalized O157 STEC cases were divided into those persons who did not visit a physician (category 1) and those who visited a physician (category 2) by estimating the physician visit rate for nonhospitalized cases. Because persons were more likely to visit a physician if they had bloody diarrhea than nonbloody diarrhea, data from outbreak investigations were used to estimate the prevalence of bloody diarrhea (50%) among nonhospitalized persons *(5)*. The proportion of nonhospitalized persons who visited a physician was then estimated separately for those with bloody diarrhea (28.0%) and nonbloody diarrhea (10.3%) using data from the Population Survey.

O157 STEC patients who visited a physician were subdivided into those whose infection was not (category 2a) or was (category 2b) laboratory diagnosed based on an estimate of the laboratory-diagnosis rate for O157 STEC outpatients (29.4%). These subcategories corresponded to the two different sources of data on patients who visited a physician (Table 1). The laboratory-diagnosis rate was estimated by dividing the number of laboratory-diagnosed O157 STEC outpatients at the FoodNet sites in 1997 *(18)* by the total number of O157 STEC outpatients at the FoodNet sites in the same year derived from the CDC estimate of the number of annual cases *(28)*.

Hospitalized O157 STEC patients who survived their illness were divided into those who did not (category 3) and those who did develop HUS based on the 1997–2002 FoodNet surveillance data on the percentage of surviving hospitalized patients who developed HUS (14.7%). Patients who developed HUS and survived were then divided into those who did not (category 4) and those who did (category 5) develop ESRD, based on information from a review of HUS patient studies *(21)* on the mean proportion of surviving patients who developed ESRD (3.3%). Fatal O157 STEC cases were divided into patients who did not (category 6) and did (category 7) develop HUS based on the 1997–2002 FoodNet data on the percentage of patients with fatal illnesses who developed HUS (62.1%).

Cost estimation. The annual cost of illness due to O157 STEC infections was estimated separately for each of the seven severity categories and then summed. The estimated costs include the costs of medical care, lost productivity, and premature deaths and are reported in 2003 dollars. Medical costs include expenditures for physician and emergency department visits, outpatient medications, and hospitalizations due to O157 STEC infections and lifetime medical care due to O157 STEC–related ESRD. Lost productivity costs include the value of time missed from work due to O157 STEC infections and reduced lifetime employment due to ESRD. The cost of premature deaths includes the cost of deaths from an O157 STEC infection and reduced life expectancy due to ESRD. The estimated costs of lifetime medical care, lost productivity, and premature deaths were adjusted for differences in patient age.

The data sources used to estimate the cost per case for each severity category are shown in Table 1. FoodNet case-control study and Population Survey respondents who were still ill when interviewed were excluded from the estimates, except when measuring time missed from work by case-control study respondents because there was sufficient information about the duration of illness to model their return to work using survival analysis to adjust for data censoring. Because no data were available on the medical or productivity costs for fatal cases (categories 6 and 7) or for HUS patients who developed ESRD (category 5) during the acute phase of their illness, these costs were assumed to be the same as for patients from the most similar severity category with data (Table 1). The age distribution of individuals in each severity category was obtained from FoodNet data, except for HUS patients who developed ESRD (category 5). HUS patients who developed ESRD were assumed to have a log normal age distribution with a mean of 2.4 years and a range of 0 to 18 years, using information from the review of HUS patient studies *(21).*

Medical costs: physician and emergency department visits due to O157 STEC infections. The costs of physician and emergency department visits for O157 STEC infections in categories 2 through 4 were determined from the average number of visits per patient for each category and the average cost per visit. The average cost of a physician office visit was estimated from 2000 National Health Accounts data on physician and clinical services expenditures *(11)* and 2000 American Medical Association data on the number of office-based physicians and patient visits *(33, 45).* Expenditures were adjusted to exclude services other than physician office visits and updated to $102.80 per visit (in 2003 dollars) using the Consumer Price Index (CPI) for physician services *(6).* The average cost of an emergency department visit was estimated using data on emergency department visits and costs in 1987 *(38, 39)* and updated to $320.87 per visit (in 2003 dollars) using the CPI for hospital services *(6).*

Medical costs: outpatient medications for O157 STEC infections. The cost of outpatient medications for O157 STEC infections in categories 1 through 4 was determined from the proportion of cases in each category using antibiotics, antidiarrheals, or certain antiemetics and the cost of each particular medication. Neither of the FoodNet special studies asked about the amount of medication used, so respondents were assumed to have purchased only one course of prescription drugs or one retail unit of nonprescription medications. The average cost of each prescription drug was estimated based on the 2001 Medical Expenditures Panel Survey (MEPS) prescribed medicines file, which provides estimates of expenditures on prescription drugs for households *(1).* The MEPS estimates were updated to 2003 dollars using the CPI for prescription drugs *(6).* The average cost of each nonprescription medication was estimated from the average wholesale price reported by manufacturers *(37).* The mean wholesale price for retail-size units of each medication was adjusted upward by the estimated retail markup for nonprescription medications *(12)* and converted to 2003 dollars using the CPI for internal and respiratory over-the-counter drugs *(6).*

Medical costs: hospitalizations due to O157 STEC infections. The cost of hospital care due to O157 STEC infections for categories 3 through 7 was determined from the average cost of a hospitalization. Because the FoodNet case-control study asked about days spent in the hospital rather than admissions, each hospitalized patient was assumed to have been admitted only once. The average cost of a hospitalization was estimated using the 2001 Nationwide Inpatient Sample file, which provides total charges and *International Classification of Diseases, 9th Revision* (ICD-9) diagnosis codes for community hospital admissions *(3).* Admissions with a principal diagnosis of enterohemorrhagic *E. coli* infection (ICD-9 008.04) but without a secondary diagnosis of HUS (ICD-9 283.11) were used to estimate the cost for categories 3 and 6. Admissions with a principal diagnosis of HUS or with a principal diagnosis of enterohemorrhagic *E. coli* infection and a secondary diagnosis of HUS were used to estimate the costs for categories 4, 5, and 7.

The hospital charges recorded in the Nationwide Inpatient Sample file exceed the payments actually received by hospitals because health plans negotiate substantial price discounts for their enrollees. The estimated charges for O157 STEC cases were therefore converted to costs by multiplying each estimate by the average cost-to-charge ratio for U.S. hospitals in 2001, which was 0.454. This ratio was obtained by weighting the reported hospital cost-to-charge ratios for the urban and rural areas of individual states in 2001 by the number of hospital admissions in each area *(22, 23).*

Charges from the Nationwide Inpatient Sample file exclude the cost of physician services billed separately from hospital services. These additional costs were estimated using the 2001 MEPS hospital inpatient stays file, which provides estimates of expenditures on hospital inpatient care for households classified by whether payments were made to hospitals or physicians *(2).* The ICD-9 diagnosis codes on the MEPS file were not detailed enough to identify O157 STEC cases, so payments to physicians were assumed to equal the physician share of payments for all hospitalizations, which was 17.3%. The estimated cost of a hospitalization was then updated to $4,681.09 per admission without an HUS diagnosis and $30,307.30 per admission with an HUS diagnosis (in 2003 dollars) using the inpatient hospital services CPI and the physician services CPI *(6).*

Medical costs: lifetime medical care due to ESRD. The lifetime cost of medical care due to ESRD for category 5 was estimated using data on the U.S. ESRD population *(40).* The present distribution of medical costs for the ESRD population by age and treatment mode was assumed to be the schedule of costs that ESRD patients would incur during their lifetime as they aged and alternated between kidney dialysis and a functioning kidney transplant. Information about medical costs was obtained from 1997 through 2001 data on ESRD expenditures by the Medicare program, which covers most ESRD patients *(40)*. The future period during which ESRD patients would incur costs was determined by calculating an abridged life table providing age-specific life expectancies for the ESRD population from 2001 data on ESRD patients and deaths by age *(40)*. The age-specific mean annual expenditures per ESRD patient were averaged across treatment mode, adjusted upward to include expenditures by other payers using the ratio of total ESRD medical costs to Medicare ESRD costs, and updated to 2003 dollars using the CPI for medical care *(6)*. The present value of future medical costs for ESRD patients was then estimated by summing the age-specific expenditures over the life expectancy of patients from the age they became ill, using a 3% annual discount rate.

Lost productivity costs: time missed from work due to O157 STEC infections. The cost of time missed from work due to O157 STEC infections for categories 1 through 4 was determined from the average number of work days lost per employed individual, the employment rate for each category, and the average daily productivity per worker, using two age groups (15 through 39 years and ≥40 years). The FoodNet case-control study and Population Survey asked about only the number of days when employed respondents missed more than half of a day of work because of their illness, so each missed day was assumed to equal three fourths of a full work day. The number of missed days could not be estimated for category 4 cases because of data limitations, so these patients were conservatively assumed to have missed as many days on average as category 3 patients. The average daily productivity of workers was estimated using March 2001 Current Population Survey data on average hourly earnings per U.S. worker in 2000 classified by age and self-employment status *(7)*. The estimated earnings were adjusted to include employer costs of benefits for employees *(8)*, and updated to $159.88 per day for workers aged 15 through 39 years and $212.43 per day for workers ≥40 years of age (in 2003 dollars) using the all-items CPI *(6)*.

Lost productivity: reduced lifetime employment due to ESRD. The cost of reduced lifetime employment due to ESRD for category 5 was estimated by comparing the age-specific employment rates for the ESRD and general U.S. populations. The difference was assumed to be the reduction in employment due to ESRD. Employment rates for ESRD dialysis patients were obtained from a national study *(13)*. Employment for ESRD transplant patients were assumed to be 83% higher than that for dialysis patients on the basis of an earlier national study *(16)*. U.S. employment rates were obtained from the March 2001 Current Population Survey *(7)*. The age-specific cost of lost productivity for the ESRD population was determined by multiplying the age-specific proportion of persons not able to work because of ESRD averaged across treatment mode by the average annual earnings per U.S. worker in 2000 from the March 2001 Current Population Survey classified by age and self-employment status, adjusted to include employer costs of benefits, and updated to 2003 dollars using the all-items CPI *(6–8)*. The present value of future lost productivity for ESRD patients was then estimated by summing the age-specific costs over the life expectancy of patients from the age when they became ill, using a 3% annual discount rate.

Costs of premature death: deaths from an O157 STEC infection. The cost of deaths from an O157 STEC infection for categories 6 and 7 was estimated using a modified value of a statistical life approach that takes age at death into account *(27)*. The value of a statistical life reflects individual risk preferences. For this study, the value of a statistical life was assumed to be the midpoint of published estimates derived from the wage differentials for jobs with higher mortality risks, or $5.0 million in December 1990 dollars at age 40 *(42)* updated to $6.9 million in 2003 dollars using the all-items CPI *(6)*. This sum was treated as if it were the value of a fixed annual annuity paid over the average U.S. life span at an interest rate of 3%. The cost of a death at any particular age is therefore the present value of life expectancy at that age. For example, average U.S. life expectancy at age 65 is 18 years *(4)*, so the value of a premature death at age 65 is determined by calculating the present value of 18 future annual annuity payments. After adjusting for age at death, the estimated cost of a premature death ranged from $9.3 million for an infant <1 year of age to $1.8 million for an adult ≥85 years of age, using the age-specific life expectancies from the 2001 U.S. life table *(4)*. The calculations of the cost of premature deaths were simplified by first grouping the deaths into 5-year age groups.

Costs of premature death: reduced life expectancy due to ESRD. The cost of reduced life expectancy due to ESRD for category 5 was estimated using the same modified value of a statistical life approach employed for deaths from an O157 STEC infection *(27)*. ESRD patients were grouped into the age categories used in the ESRD life table, and the reduction in life expectancy due to ESRD was determined for each age group by comparing the age-specific life expectancies from the ESRD life table and the 2001 U.S. life table *(4)*. The cost of the reduced life expectancy due to ESRD was then estimated by summing the present value of the future years of life lost by each age group due to the shorter average life expectancies for ESRD patients than for the general U.S. population.

RESULTS

The expansion of the CDC estimate of annual O157 STEC cases, hospitalizations, and deaths into seven severity categories is shown in Table 1. Of the estimated 73,480 annual cases, 78% of the individuals did not visit a physician, 19% visited a physician but were not hospitalized, and 3% required hospitalization. Of the estimated 2,168 hospitalized patients, 16% developed HUS, <1% developed ESRD, and 3% died. Two thirds of the patients who died had HUS.

The estimates derived from the FoodNet special studies indicate that O157 STEC individuals with more severe illnesses used more medical care and lost more time from work on average than did individuals with less severe illnesses (Table 2). Overall, annual medical care for O157 STEC cases was estimated to include approximately 20,000 physician visits, 7,500 emergency department visits, 1,820 hospitalizations without an HUS diagnosis, and 348 hospitalizations with an HUS diagnosis. O157 STEC individuals also used an estimated 5,500 courses of prescription medications and 24,700 retail units of nonprescription medication on an outpatient basis. In addition, employed O157 STEC individuals lost an estimated 24,200 days from work each year.

Most of the prescription medications used by O157 STEC individuals were antibiotics. About one half of the nonprescription medications were antimotility agents for slowing intestinal peristalsis. Patients who visited a physician but were not hospitalized used most of the prescription medications and made most of the physician visits and

TABLE 2. *Estimated use of medical care and time lost from work per O157 STEC infection, FoodNet sites*[a]

Severity category	Mean (SE) no. of physician visits per person	Mean (SE) no. of emergency department visits per person	Mean (SE) no. of courses of outpatient prescription medication per person	Mean (SE) no. of retail units of outpatient nonprescription medication per person	Mean (SE) no. of days missed from work per employed person
1. Did not visit a physician[b]	NA	NA	0.01 (0.005)	0.31 (0.02)	0.25 (0.05)
2a. Visited a physician, O157 STEC infection not laboratory diagnosed[b]	1.23 (0.12)	0.32 (0.08)	0.13 (0.05)	0.44 (0.08)	2.81 (1.36)
2b. Visited a physician, O157 STEC infection laboratory diagnosed[c]	1.37 (0.10)	0.60 (0.05)	0.54 (0.04)	0.56 (0.05)	2.91 (0.66)
3. Hospitalized, did not develop HUS[c]	1.02 (0.13)	0.88 (0.05)	0.59 (0.07)	0.60 (0.06)	7.13 (1.51)
4. Hospitalized, developed HUS but not ESRD[c]	1.93 (0.40)	1.27 (0.25)	0.44 (0.22)	0.75 (0.21)	—[d]

[a] SE, standard error of the mean. Variance estimates from the 2002–2003 FoodNet Population Survey were adjusted for the complex survey sample design. Variance estimates from the 1999–2000 FoodNet *E. coli* O157 case-control study assumed that interviewed patients were a simple random sample of all patients. STEC, Shiga toxin–producing *E. coli* O157; NA, not applicable.
[b] 2002–2003 FoodNet Population Survey estimates for persons with an acute diarrheal episode during the previous month who did not have diarrhea at the time of the interview.
[c] 1999–2000 FoodNet *E. coli* O157 case-control study estimates for patients who did not have diarrhea at the time of the interview except for estimates of days missed from work, which were based on all patients.
[d] Estimate not available because of lack of data.

emergency department visits. Persons who did not visit a physician used most of the nonprescription medications. The average cost of the medications used by O157 STEC individuals was estimated to be $50.13 per course of prescription medication and $7.34 per retail unit of nonprescription medication.

The estimated annual cost of illness due to O157 STEC from all sources of infection was $405 million (in 2003 dollars), including $370 million for premature deaths, $30 million for medical care, and $5 million for lost productivity (Table 3). The average cost of an O157 STEC case varied greatly by severity category, ranging from $26 for

TABLE 3. *Estimated annual economic cost of illness due to O157 STEC infections, United States*[a]

Cost category	Severity category: 1. Did not visit a physician	2. Visited a physician	3. Hospitalized, did not develop HUS	4. Hospitalized, developed HUS but not ESRD	5. Hospitalized, developed HUS and ESRD	6. Died, did not develop HUS	7. Died, developed HUS	All cases
O157 STEC infections								
Medical care	0.1	3.7	9.2	9.3	0.3	0.1	1.2	24.0
Phsician visits	NA	1.8	0.2	0.1	0.0[b]	0.0[b]	0.0[b]	2.0
Emergency department visits	NA	1.8	0.5	0.1	0.0[b]	0.0[b]	0.0[b]	2.4
Hospitalizations	NA	NA	8.4	9.1	0.3	0.1	1.2	19.1
Outpatient medications	0.1	0.2	0.1	0.0[b]	0.0[b]	0.0[b]	0.0[b]	0.5
Lost productivity	1.3	2.3	0.9	0.0[b]	0.0	0.0[b]	0.0[b]	4.5
Premature deaths	NA	NA	NA	NA	NA	91.8	233.5	325.3
Subtotal	1.5	6.0	10.1	9.3	0.3	92.0	234.7	353.8
End-stage renal disease								
Medical care	NA	NA	NA	NA	6.2	NA	NA	6.2
Lost productivity	NA	NA	NA	NA	0.5	NA	NA	0.5
Premature deaths	NA	NA	NA	NA	44.7	NA	NA	44.7
Subtotal	NA	NA	NA	NA	51.4	NA	NA	51.4
Total	1.5	6.0	10.1	9.3	51.7	92.0	234.7	405.2
Average cost per case[c]	26	441	5,599	30,998	5,173,594	3,998,265	6,175,500	5,515

[a] Estimated costs (in millions of 2003 dollars) may not sum to reported totals and percentages may not sum to 100.0 because of rounding. STEC, Shiga toxin–producing *E. coli* O157; HUS, hemolytic uremic syndrome; ESRD, end-stage renal disease; NA, not applicable.
[b] Estimated cost <$0.1 million.
[c] Estimate in dollars calculated from unrounded totals.

an individual who did not visit a physician to $6.2 million for a patient who developed HUS and died. Although only a small proportion of O157 STEC infections resulted in ESRD or death, these severe cases were responsible for 93% of the total cost, or $378 million.

The principal cost of O157 STEC infections varied by severity category. Most of the cost for individuals who did not visit a physician was due to lost productivity. Expenditures on medical care were the principal cost for patients who visited a physician but were not hospitalized, hospitalized patients who did not develop HUS, and hospitalized patients who developed HUS but not ESRD. Nearly all of the cost for ESRD and fatal cases was due to premature deaths. The average cost of a premature death was higher for patients who developed HUS ($6.2 million) and died than for other patients who died ($4.0 million) because 50% of HUS deaths, but only 10% of other deaths, were children <15 years old.

DISCUSSION

The estimated annual cost of illness due to O157 STEC infections acquired from food or other sources was $405 million (in 2003 dollars), including the costs of medical care, lost productivity, and premature deaths. This estimate is less than the lower bound of the earlier ERS cost estimate *(9)*, which was approximately $0.5 to $3.3 billion (in 2003 dollars). The estimates differ because there were numerous differences in assumptions and methods between the two studies. The main reason why the present estimate is lower is because the earlier study assumed that there were substantially more fatal cases than were assumed in the present study, which was based on the CDC estimate of annual O157 STEC infections released after the earlier study was completed *(28)*. Although the two studies employed different methodologies to value premature deaths, the present study assigned a higher average value per premature death than the earlier study. The present study also provides a more reliable estimate of the medical and productivity costs per case because information about medical care and time lost from work by O157 STEC individuals was obtained from the population-based FoodNet surveillance system. In contrast, the earlier study relied on data from published case series and outbreak reports, which are unlikely to be a representative sample of O157 STEC cases.

The cost of illness represents only part of the costs due to O157 STEC infections. Some of the other costs omitted by both the present study and the earlier ERS study include pain and suffering, government and business expenditures in response to outbreaks of illness, and spending on research to prevent future infections. These costs also must be estimated to determine the total cost of O157 STEC infections.

Although fewer than one of every thousand O157 STEC infections resulted in chronic ESRD or death, these severe cases accounted for 93% of the estimated cost of illness. Most of the cost for severe cases was the cost of premature deaths. Because the cost of premature deaths is such a large share of the estimated cost of O157 STEC, alternate assumptions about the value of a statistical life could have a significant effect on the estimated cost. For example, the U.S. Food and Drug Administration (FDA) assumes that the value of a statistical life is $5.0 million *(17)*, in comparison to the inflation-adjusted value of $6.9 million used in this study. If this study had used the lower FDA value, the estimated cost of O157 STEC would have been reduced by 25%, or $101 million.

The cost of foodborne O157 STEC infections is the potential economic benefit from preventing such infections. The CDC has estimated that 85% of O157 STEC infections are foodborne in origin *(28)*. If foodborne infections are as costly as other O157 STEC infections, then about $344 million of the annual cost of illness from this pathogen can be attributed to contaminated food.

The estimated cost of foodborne O157 STEC infections could be used to assess the effectiveness of regulatory measures to control O157 STEC in the U.S food supply. During the past decade, the federal government classified *E. coli* O157:H7 in raw ground beef as an adulterant, began testing ground beef samples for *E. coli* O157:H7 contamination, and required firms to place safe handling labels on raw meat and poultry and warning labels on unpasteurized juice *(31)*. The federal government also implemented hazard analysis and critical control point (HACCP) programs to control foodborne pathogens in meat and poultry plants and the juice industry and subsequently directed beef producers to reassess whether their HACCP plans prevented *E. coli* O157:H7 contamination *(31, 43)*. Beef producers have collaborated to identify effective methods to control *E. coli* O157:H7 *(14)*, and many have recently begun releasing production lots of raw ground beef only if they have tested negative for *E. coli* O157:H7 *(43)*. These measures increased costs for producers, sometimes by a substantial amount. For example, in 2003 the HACCP program raised annual production costs for beef producers by an estimated 1.2 cents per pound (2.6 cents per kg) *(31)*, or about $310 million overall *(30)*. The question of whether the economic cost of a particular regulatory measure such as a HACCP program exceeds the benefits could be answered by conducting a cost-benefit analysis. Some of the information needed for such an analysis is the cost of implementing the measure, the cumulative number of O157 STEC infections averted by the measure, and the estimated average cost per O157 STEC case as reported here.

This study had several limitations. One was the uncertainty about the annual number of O157 STEC cases. The CDC estimate of annual cases was extrapolated from the incidence of laboratory-diagnosed O157 STEC infections in the FoodNet surveillance sites in 1997 *(28)*, which is subject to several kinds of potential error. In another study that used the FoodNet surveillance data to characterize the uncertainty, the authors concluded that there were 75,000 annual O157 STEC cases in 1998, with a 95% confidence interval (CI) of 50,000 to 120,000 cases, including 1,200 to 2,400 hospitalizations and 25 to 90 deaths *(34)*. Using this alternative estimate of cases, the 95% CI for the annual cost of O157 STEC would be $182 to $572 million.

Because the CDC estimate of annual O157 STEC cases was based on the incidence of laboratory-diagnosed infections in 1997, it may be outdated. Recent data indicate that the incidence of laboratory-diagnosed O157 STEC infections in the FoodNet surveillance sites decreased by 46% between the 1996 to 1998 period and 2004, with most of the decline occurring after 2002 *(44).* The large decline in the incidence of O157 STEC in the FoodNet sites suggests that the national incidence has also declined. However, it is unclear whether the national decline was as great as the reduction in the FoodNet sites or whether the distribution of cases by severity was affected. When a more precise estimate of annual O157 STEC cases classified by severity becomes available, the estimated cost of illness could be readily updated using the estimated average cost per case by severity as reported here.

Another limitation of this study is the unknown sensitivity of the passive surveillance for adult HUS cases in the FoodNet sites *(19).* Passive disease surveillance systems tend to underestimate the number of cases. Adult HUS cases that were not detected by passive surveillance would have been misclassified as non-HUS cases, affecting the estimated cost of O157 STEC because HUS cases are more costly. The potential effect of misclassification on the cost estimate was assessed by arbitrarily assuming that passive surveillance detected only half of the adult HUS cases in the FoodNet sites. After correcting the classification of O157 STEC cases by severity for the assumed undercount of HUS cases, the estimated cost of O157 STEC was increased by only 2%, or $6 million. The cost increase was minimal because there was no change in the cost of premature deaths, and other costs that were relatively higher for HUS cases than non-HUS cases represented only a small share of the total cost. This simulation suggests that incomplete surveillance for adult HUS cases did not seriously bias the cost estimate.

This study relied on other assumptions about O157 STEC infections that may not be accurate. For example, O157 STEC persons who did not visit a physician and patients who visited a physician but were not laboratory diagnosed were assumed to incur the same medical and productivity costs as FoodNet Population Survey respondents who had acute diarrhea. Similarly, the future lifetime costs for O157 STEC patients who developed ESRD were assumed to equal the current costs for the ESRD population, and the risk of HUS patients developing ESRD was assumed to equal the mean proportion of ESRD cases in HUS patient studies. Future investigations of the health burden due to O157 STEC infections could reduce the need for such assumptions by gathering more information about individuals who did not visit a physician, other patients whose infections were not laboratory confirmed, and ESRD patients. Despite these limitations, the results of this study indicate that O157 STEC infections are costly for society. The high cost of illness due to O157 STEC suggests that additional efforts to prevent infections by this pathogen might be warranted.

ACKNOWLEDGMENTS

P. D. Frenzen thanks Todd Wagner for advice about hospital cost-to-charge ratios, Tim Covington for information about nonprescription drug prices, and Elise Golan and two anonymous reviewers for helpful comments on an earlier version of the manuscript.

REFERENCES

1. Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. 2004. MEPS HC-059A: 2001 prescribed medicines file. Available at: http://www.meps.ahrq.gov/Puf/PufDetail.asp?ID=149. Accessed 24 September 2004.
2. Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. 2004. MEPS HC-059D: 2001 hospital inpatient stays file. Available at: http://www.meps.ahrq.gov/Puf/PufDetail.asp?ID=148. Accessed 29 September 2004.
3. Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. 2004. Overview of the Nationwide Inpatient Sample (NIS). Available at: http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed 27 September 2004.
4. Arias, E. 2004. United States life tables, 2001. *Natl. Vital Stat. Rep.* 52:1–40.
5. Bender, J. B., K. E. Smith, A. A. McNees, T. R. Rabatsky-Ehr, S. D. Segler, M. A. Hawkins, N. L. Spina, W. E. Keene, M. H. Kennedy, T. J. Van Gilder, and C. W. Hedberg. 2004. Factors affecting surveillance data on *Escherichia coli* O157 infections collected from FoodNet sites, 1996–1999. *Clin. Infect. Dis.* 38(Suppl. 3):S157–S164.
6. Bureau of Labor Statistics, U.S. Department of Labor. 2004. Consumer price indexes. Available at: http://www.bls.gov/cpi/home.htm. Accessed 6 April 2004.
7. Bureau of Labor Statistics, U.S. Department of Labor. 2004. CPS annual demographic survey March supplement: 2001 methodology and documentation. Available at: http://www.bls.census.gov/cps/ads/2001/smethdoc.htm. Accessed 6 October 2004.
8. Bureau of Labor Statistics, U.S. Department of Labor. 2004. National compensation survey—compensation cost trends. Available at: http://www.bls.gov/ncs/ect/home.htm#overview. Accessed 17 June 2004.
9. Buzby, J. C., and T. Roberts. 1996. ERS updates U.S. foodborne disease costs for seven pathogens. *Food Rev.* 19:20–25.
10. Buzby, J. C., T. Roberts, C.-T. Jordan Lin, and J. M. MacDonald. 1996. Bacterial foodborne disease: medical costs and productivity losses. Agricultural Economics Report no. 741. Economic Research Service, U.S. Department of Agriculture, Washington, D.C.
11. Centers for Medicare and Medicaid Services, U.S. Department of Health and Human Services. 2004. Health accounts. Available at: http://www.cms.hhs.gov/statistics/nhe/default.asp. Accessed 10 November 2004.
12. Covington, T. R. 2002. The pharmacist as nonprescription drug therapy manager. *J. Am. Pharm. Assoc.* 42:518–519.
13. Curtin, R. B., E. T. Oberley, P. Sacksteder, and A. Friedman. 1996. Differences between employed and nonemployed dialysis patients. *Am. J. Kidney Dis.* 27:533–540.
14. *E. coli* Summit Task Force. 2003. A summit's summary. *Meat Process. Mag.* Available at: http://www.meatnews.com/mp/northamerican/dsp_article_mp.cfm?artNum=466. Accessed 8 November 2004.
15. Ebel, E., W. Sclosser, J. Kause, K. Orloski, T. Roberts, C. Narrod, S. Malcolm, M. Coleman, and M. Powell. 2004. Draft risk assessment of the public health impact of *Escherichia coli* O157:H7 in ground beef. *J. Food Prot.* 67:1991–1999.
16. Evans, R. W., D. L. Manninen, L. P. Garrison, L. G. Hart, C. R. Blagg, R. A. Gutman, A. R. Hull, and E. G. Lowrie. 1985. The quality of life of patients with end-stage renal disease. *N. Engl. J. Med.* 312:553–559.
17. Food and Drug Administration, U.S. Department of Health and Human Services. 1999. 21 CFR parts 16, 101, and 115. Preliminary regulatory impact analysis and initial regulatory flexibility analysis of the proposed rule to require refrigeration of shell eggs at retail and safe handling labels. *Fed. Regist.* 64:36516–36539.
18. Foodborne Diseases Active Surveillance Network (FoodNet). 1998. 1997 FoodNet annual report. Available at: http://www.cdc.gov/foodnet/annuals.htm. Accessed 4 November 2004.
19. Foodborne Diseases Active Surveillance Network (FoodNet). 2002.

2002 FoodNet annual report. Available at: http://www.cdc.gov/foodnet/annuals.htm. Accessed 4 November 2004.

20. Fratamico, P. M., J. L. Smith, and R. L. Buchanan. 2002. *Escherichia coli*, p. 79–101. *In* D. O. Cliver and H. P. Riemann (ed.), Foodborne diseases, 2nd ed. Academic Press, London.
21. Garg, A. X., R. S. Suri, N. Barrowman, F. Rehman, D. Matsell, M. P. Rosas-Arellano, M. Salvadori, R. B. Haynes, and W. F. Clark. 2003. Long-term renal prognosis of diarrhea-associated hemolytic uremic syndrome: a systematic review, meta-analysis, and meta-regression. *JAMA* 290:1360–1370.
22. Health Care Financing Administration, U.S. Department of Health and Human Services. 2001. Medicare program; changes to the hospital inpatient prospective payment systems and fiscal year 2002 rates. *Fed. Regist.* 66:22645–22891.
23. Health Resources and Services Administration, U.S. Department of Health and Human Services. 2003. Area resource file (ARF), February 2003 release. (electronic database.) Available at: http://www.arfsys.com/. Accessed 26 October 2004.
24. Hussein, H. S., and T. Sakuma. 2005. Shiga toxin–producing *Escherichia coli*: pre- and postharvest control measures to ensure safety of dairy cattle products. *J. Food Prot.* 68:199–207.
25. Imhoff, I., D. Morse, B. Shiferaw, M. Hawkins, D. Vugia, S. Lance-Parker, J. Hadler, C. Medus, M. Kennedy, M. R. Moore, and T. Van Gilder. 2004. Burden of self-reported acute diarrheal illness in FoodNet surveillance areas, 1998–1999. *Clin. Infect. Dis.* 38(Suppl. 3):S219–S226.
26. Kennedy, M., T. Rabatsky-Ehr, S. Thomas, S. Lance-Parker, J. Mohle-Boetani, K. Smith, W. Kenne, P. Sparling, F. Hardnett, P. Mead, and the EIP FoodNet Working Group. 2002. Risk factors for sporadic *Escherichia coli* O157:H7 in the United States: a case-control study in FoodNet sites, 1999–2000. Available at: http://www.cdc.gov/foodnet/pub/iceid/2002/kennedy_m.htm. Accessed 8 November 2004.
27. Mauskopf, J. A., and M. T. French. 1991. Estimating the value of avoiding morbidity and mortality from foodborne illness. *Risk Anal.* 11:619–631.
28. Mead, P. M., L. Slutsker, V. Dietz, L. F. McCaig, J. S. Bresee, C. Shapiro, P. M. Griffin, and R. V. Tauxe. 1999. Food-related illness and death in the United States. *Emerg. Infect. Dis.* 5:607–625.
29. Meng, J., M. P. Doyle, T. Zhao, and S. Zhao. 2001. Enterohemorrhagic *Escherichia coli*, p. 193–213. *In* M. P. Doyle, L. R. Beuchat, and T. J. Montville (ed.), Food microbiology: fundamentals and frontiers, 2nd ed. ASM Press, Washington, D.C.
30. National Agricultural Statistics Service, U.S. Department of Agriculture. 2004. Livestock slaughter, January 2004. National Agricultural Statistics Service, U.S. Department of Agriculture, Washington, D.C.
31. Ollinger, M., and V. Mueller. 2003. Managing for safer food: the economics of sanitation and process controls in meat and poultry plants. Agricultural Economics Report no. 817. Economic Research Service, U.S. Department of Agriculture, Washington, D.C.
32. ORC Macro. 2003. FoodNet population survey 2002–2003. Final methodology report. ORC Macro, Burlington, Vt.
33. Pasko, T., and B. Seidman. 2002. Physician characteristics and distribution in the U.S.: 2002–2003 edition. American Medical Association, Chicago.
34. Powell, P., E. Ebel, and W. Schlosser. 2001. Considering uncertainty in comparing the burden of illness due to foodborne microbial pathogens. *Int. J. Food Microbiol.* 69:209–215.
35. Remington, P. L., M. Y. Smith, D. F. Williamson, R. F. Anda, E. M. Gentry, and G. C. Hogelin. 1988. Design, characteristics, and usefulness of state-based behavioral risk factor surveillance: 1981–87. *Public Health Rep.* 103:366–375.
36. Steeh, C., N. Kirgis, B. Cannon, and J. DeWitt. 2001. Are they really as bad as they seem? Nonresponse rates at the end of the twentieth century. *J. Off. Stat.* 17:227–247.
37. Thomson PDR Editorial Staff. 2004. Red book: pharmacy's fundamental reference, 2004 ed. Thomson PDR, Montvale, N.J.
38. Tyrance, P. H., D. U. Himmelstein, and S. Woolhandler. 1996. U.S. emergency department costs: no emergency. *Am. J. Public Health* 86:1527–1531.
39. U.S. Bureau of the Census. 1991. Statistical abstract of the United States: 1991. U.S. Bureau of the Census, Washington, D.C.
40. U.S. Renal Data System. 2003. 2003 annual data report. Available at: http://www.usrd.org/adr.htm. Accessed 13 May 2004.
41. Varma, J. K., K. D. Greene, M. E. Reller, S. M. DeLong, J. Trottier, S. F. Nowicki, M. DiOrio, E. M. Koch, T. L. Bannerman, S. T. York, M. A. Lambert-Fair, J. G. Wells, and P. S. Mead. 2003. An outbreak of *Escherichia coli* O157 infection following exposure to a contaminated building. *JAMA* 290:2709–2712.
42. Viscusi, W. K. 1993. The value of risks to life and health. *J. Econ. Lit.* 31:1912–1946.
43. Vugia, D., A. Cronquist, J. Hadler, P. Blake, D. Blythe, K. Smith, D. Morse, P. Cieslak, T. Jones, D. Goldman, J. Guzewich, F. Angulo, P. Griffin, R. Tauxe, and K. Kretsinger. 2004. Preliminary FoodNet data on the incidence of infection with pathogens commonly transmitted through food—selected sites, United States, 2003. *Morb. Mortal. Wkly. Rep.* 53:338–343.
44. Vugia, D., A. Cronquist, J. Hadler, M. Tobin-D'Angelo, D. Blythe, K. Smith, K. Thornton, D. Morse, P. Cieslak, T. Jones, R. Varghese, J. Guzewich, F. Angulo, P. Griffin, R. Tauxe, and J. Dunn. 2005. Preliminary FoodNet data on the incidence of infection with pathogens commonly transmitted through food—10 sites, United States, 2004. *Morb. Mortal. Wkly. Rep.* 54:352–356.
45. Wassenaar, J. D., and S. L. Thran. 2001. Physician socioeconomic statistics: 2000–2002 edition: profiles for detailed specialties, selected states, and practice arrangements. American Medical Association, Chicago.