The Economic Burden of Non–Influenza-Related Viral Respiratory Tract Infection in the United States

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Background: Viral respiratory tract infection (VRTI) is the most common illness in humans. Despite the high incidence, the economic impact of non–influenza-related VRTI has not been rigorously explored. Our objectives were to obtain an updated incidence of non–influenza-related VRTI in the United States and to quantify the health care resource use (direct costs) and productivity losses (indirect costs) associated with these infections.

Methods: A nationwide telephone survey of US households (N=4051) was conducted between November 3, 2000, and February 12, 2001 to obtain a representative estimate of the self-reported incidence of non–influenza-related VRTI and related treatment patterns. Direct treatment costs measured included outpatient clinician encounters, use of over-the-counter and prescription drugs, and associated infectious complications of non–influenza-related VRTI. Absenteeism estimates for infected individuals and parents of infected children were extrapolated from National Health Interview Survey data.

Results: Of survey respondents, 72% reported a non–influenza-related VRTI within the past year. Respondents who experienced a self-reported non–influenza-related VRTI averaged 2.5 episodes annually. When these rates are extrapolated to the entire US population, approximately 500 million non–influenza-related VRTI episodes occur per year. Similarly, if the treatment patterns reported by the respondents are extended to the population, the total economic impact of non–influenza-related VRTI approaches $40 billion annually (direct costs, $17 billion per year; and indirect costs, $22.5 billion per year).

Conclusions: Largely because of the high attack rate, non–influenza-related VRTI imposes a greater economic burden than many other clinical conditions. The pending availability of effective antiviral therapies warrants increased attention be paid to this common and expensive illness.

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RESPIRATORY TRACT infection is the most common illness in humans. Largely because of the high attack rate, respiratory tract infections are associated with significant patient morbidity and related mortality. In developing countries, morbidity due to respiratory tract infections may be at least as severe as that in industrialized countries; for children younger than 5 years, these infections are the leading cause of death.[1]

Viruses are the causal pathogen in most upper respiratory tract infection cases, with fewer than 10% of the cases caused by bacteria.[2] The viral pathogens primarily associated with upper respiratory tract infections include picornaviruses (notably, rhinoviruses and enteroviruses), coronaviruses, adenoviruses, parainfluenza viruses, influenza viruses, and respiratory syncytial viruses.[1,3] Picornaviruses are present year-round and, thus, contribute significantly to the incidence of viral respiratory tract infections (VRTIs), particularly in the fall and early spring.[4] Influenza, a potentially more serious illness that usually occurs during the winter, accounts for 9% of total upper respiratory tract illnesses and 13% of upper respiratory tract illnesses that lead to physician consultation.[5] While the clinical issues relevant to non–influenza-related VRTIs have been studied, to our knowledge, the economic impact of these infections has not been rigorously explored.

The morbidity associated with non–influenza-related VRTI is not trivial. The median duration of an episode is 7.4 days, with 25% of cases lasting 2 weeks.[6] Viral respiratory tract infections due to picornaviruses, in particular, produce more restriction of activity and physician consultation than respiratory illnesses caused by other viruses or bacteria.[7,8] More specifically, the 1996 report[9] from the National

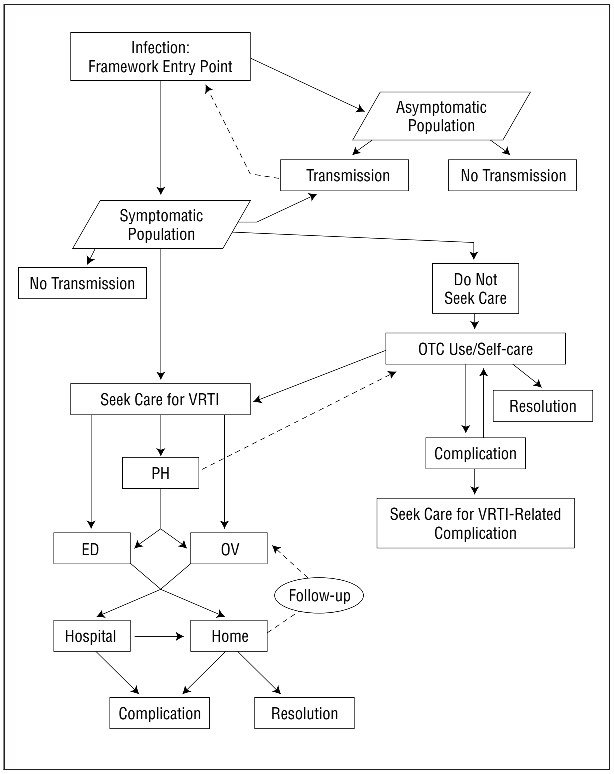

Figure 1. Conceptual model of potential costs attributable to viral respiratory tract infection (VRTI). A complication is defined as a respiratory exacerbation, otitis media, sinusitis, or a lower respiratory tract infection. OTC indicates over-the-counter; PH, telephone contact with a physician; ED, emergency department; and OV, office visit.

Center for Health Statistics estimates that VRTI causes approximately 20 million lost workdays in adults and 21 million lost school days in children annually.

The burden of VRTI is even more pronounced in individuals with chronic comorbidities or clinical risk factors, including those with asthma and chronic obstructive pulmonary disease, elderly patients,[10,11] those with a history of otitis media[12-15] or sinusitis,[16-18] and those who are immunocompromised.[19-25] Asthmatic children experience more VRTIs than nonasthmatic children, with up to 45% of acute asthma exacerbations thought to be related to VRTI. Viral respiratory tract infections due to picornaviruses have been implicated as a major contributor to asthma exacerbations in children[26-31] and, to a lesser extent, in adults.[10,32,33]

Despite this substantial level of morbidity, non–influenza-related VRTI does not receive a similar amount of attention when compared with less common clinical conditions. At least 2 factors contribute to this indifference. First, the aggregate clinical and economic consequences resulting from VRTI and/or its complications have not been well studied. Second, there are no available medications that treat the cause of the common cold. Notably, innovative antiviral therapies are under investigation or under review by the US Food and Drug Administration; they may provide physicians and the public with the first agents to treat the causal agents.

The promise of effective antiviral agents warrants a rigorous estimate of the economic impact of the common cold. Accordingly, our objectives were to obtain an updated incidence of non–influenza-related VRTI in the United States and to quantify the economic impact of health care resource use (direct costs) and productivity losses (indirect costs) associated with these infections.

METHODS

To rigorously estimate the economic burden of the common cold, a 3-step process was used. First, a conceptual model was developed to determine which costs (direct and indirect) are potentially attributable to symptomatic episodes. Second, non–influenza-related VRTI incidence and health care use were determined from a comprehensive epidemiological survey of US households. Once incidence and treatment patterns were elicited, unit cost estimates were obtained from a synthesis of published literature and secondary data sources. These same data sources were used to estimate associated indirect costs.

CONCEPTUAL MODEL OF POTENTIAL COSTS ATTRIBUTABLE TO VRTI

A conceptual model depicting VRTI natural history and possible management options was constructed to direct the measurement of resources that could be potentially used by a person (or his or her caregiver) with a symptomatic episode (**Figure 1**). This conceptual model was derived from a comprehensive review of published literature evaluating the pathogenesis, clinical presentation, clinical course, risk factors, and patterns of care. The pathway was reviewed and modified by a 14-member expert panel consisting of 6 respiratory specialists, 3 primary care clinicians (A.M.F. and others), 2 pediatricians, 2 infectious disease specialists, and 1 otolaryngology specialist.

PRIMARY DATA COLLECTION: NON–INFLUENZA-RELATED VRTI INCIDENCE AND ASSOCIATED HEALTH CARE USE

To obtain a more recent and representative estimate of the incidence of non–influenza-related VRTI in the United States and to determine patterns of care for those with colds, a nationwide survey of US households was conducted between November 3, 2000, and February 12, 2001. An unrestricted random sampling method (random digit–dial) was used to minimize bias found in systematic sampling procedures. The survey was administered using a computer-assisted telephone interviewing system to optimize accuracy of data collection and entry.

Only adults (defined as persons 18 years or older) who were willing to respond to the survey were included in the sample. Questions focused on the number of colds the respondent (and/or child) experienced during the past 12 months and specific ways in which the respondent treated the illness. Adult respondents were first asked questions about their non–influenza-related VRTI "cold" history, followed by questions regarding the history of the child in the family with the most recent episode (if applicable). A cold was defined in the survey as "having symptoms such as stuffy or runny nose, sore/scratchy throat, sneezing, with little or no fever and usually lasting about 1 week . . . not referring to 'the flu,' which is usually characterized by high fever, headache, overall body aches, pains, and weakness."

Respondents who had experienced a symptomatic VRTI episode were asked specific questions aimed at quantifying health care use and self-care practices. These questions provided data regarding the frequency of use for over-the-counter (OTC) medications, the frequency of telephone calls to a physician, the frequency of outpatient physician visits, and the use of prescription medications (eg, antibiotics and symptomatic treatments). Respondents were further asked to list the prescription medications received during their most recent episode. Specific OTC medications were not elicited.

SECONDARY DATA SYNTHESIS: COMPLICATIONS OF NON–INFLUENZA-RELATED VRTI AND COST MEASUREMENT

Estimates of the frequency of physician encounters through an emergency department and the occurrence of VRTI-related complications, including acute sinusitis, otitis media, and lower respiratory tract infections, were obtained from the published literature and from pooled data generated from several randomized clinical trials-.[34,35] Estimates of absenteeism (for the person with the cold and the caregiver) were extrapolated using data from the National Health Interview Survey (NHIS) and the Bureau of Labor Statistics.

To quantify the unit costs for each use variable, data from the literature and from publicly available databases, including the US Census, the NHIS, the Medical Expenditure Panel Survey, and the National (Hospital) Ambulatory Medical Care Survey, were used.

Direct Medical Costs

Unit cost data for outpatient physician visits, physician encounters in an emergency department, and the treatment of acute sinusitis, otitis media, and lower respiratory tract infections were obtained from the 1997 Medical Expenditure Panel Survey database. The Medical Expenditure Panel Survey database contains cost estimates composed of physician service costs and diagnostic/laboratory testing costs. The value for each type of physician encounter was calculated using the average insurance payment (not the charged amount). The average cost per complication associated with non–influenza-related VRTI was calculated by weighing the cost of each type of physician encounter by the proportion of patients who use the respective type of encounter. The cost of a telephone physician encounter was assumed to be $0.

No source was identified reporting OTC cost figures specific to non–influenza-related VRTI. As a result, a per-episode cost of $8.31 (range, $5.58-$11.04) was included for individuals who reported purchasing an OTC product for their non–influenza-related VRTI. This estimate was based on the retail costs of a market basket of 10 popular cold and flu medications, including NyQuil, Tylenol Cold & Flu, Advil Cold & Sinus, Sudafed Cold & Cough, Children's Dimetapp, Coricidin D, Aleve Cold and Sinus, and Alka-Seltzer Cold & Sinus. The low cost estimate ($5.58, or a 33% reduction) reflects the cost of similar products purchased as generic (instead of brand name) cough and cold remedies.

To estimate the unit cost incurred for prescription medications, the typical dosing regimen for each medication listed by respondents was determined. To this dose, a unit cost per regimen was applied using published average wholesale price lists.[36] A weighted-average cost per prescription was calculated based on the regimen price and relative distribution of medication use across the therapeutic class (antibiotics and symptomatic therapies). All cost estimates were converted to 2001 US dollar values using inflation adjustments from the Bureau of Labor Statistics.

Indirect Costs

Missed Caregiver Workdays. Missed caregiver workdays were defined as absenteeism of a parent or guardian secondary to a child staying home from school or day care because of a non–influenza-related VRTI. The number of missed workdays per cold was calculated using statistics from the NHIS[9] and primary data obtained from the epidemiological survey. The following assumptions were used to extrapolate the number of school days lost by the NHIS child population to the general child population with non–influenza-related VRTI. Assumption 1. Only single-parent families (with the one parent working) and dual-parent families (with both parents working) were considered. In these households, it was assumed that the number of missed school days for children aged 5 to 17 years is equal to the number of missed caregiver workdays. Assumption 2. For the fully employed households previously described, it was assumed that the proportion of missed day care or school days per cold episode for children from birth to the age of 4 years is equal to the proportion of missed school days per cold episode in children aged 5 to 17 years. This is a conservative assumption in that the incidence of non–influenza-related VRTI is higher in the younger population (birth-4 years) and it is reasonable to expect that a caregiver is at least as likely to stay home with a younger child as with an older child (aged 5-12 years). Assumption 3. Productivity cost is based on an average hourly wage of $14.35 from the Bureau of Labor Statistics[37] (2001) and an 8-hour day.

Given these assumptions, the following was estimated ($ indicates cost in US dollars; and *p*, proportion):

$$\text{Caregiver } \$ = [\text{No. of Episodes}] \times [p(\text{All-Worker Family})] \times [\$(\text{Workday})] \times [p(\text{Missed School Day})]$$

Missed Workdays (Absenteeism). The number of missed workdays per cold episode was calculated using statistics from the NHIS, data from the epidemiological survey, and the literature. As previously noted, we assumed that productivity cost due to non–influenza-related VRTI is based on an average hourly wage of $14.35 and an 8-hour day.

Given these assumptions, the following was estimated ($ indicates cost in US dollars; and *p*, proportion):

$$\text{Work Loss } \$ = [\text{No. of Episodes}] \times [\$(\text{Workday})] \times [p(\text{Missed Workday})]$$

SENSITIVITY ANALYSIS

To measure how robust our results were to changes in base case inputs, a sensitivity analysis was performed with 2 methods. First, in a Monte Carlo simulation, inputs were varied simultaneously and randomly for more than 1000 iterations, yielding a range of cost estimates when variables in the model are allowed to take on different distributions. From this simulation, a 95% confidence range was calculated for the total cost estimate and the relative importance of each input variable was determined. Second, univariate sensitivity analyses were performed around a range for each of the inputs evaluated.

The distribution of all input variables used in the model was assumed to be normal across the range of reasonably possible values. For all probabilities or percentage values (ie, use percentages), the SE assumptions used in the sensitivity calculations were derived from the following equation for a binomial variable (where p indicates proportion; and n, number of observations): $SE = \sqrt{\{[p(1-p)]/n\}}$.

RESULTS

INCIDENCE OF NON–INFLUENZA-RELATED VRTI

A total of 84 239 randomly placed telephone calls were made. Of these calls, 80 161 did not generate a usable response: 57% were not answered, 21% refused to partici-

Table 1. Demographic Characteristics of the 4051 Survey Respondents

Characteristic	% of Respondents*
Age, y	
18-29	21
30-49	40
50-65	23
>65	16
Race	
White	80
African American	9
Asian	2
Other	11
Net worth, US $	
<30 000	27
30 000-<50 000	22
50 000-100 000	31
>100 000	20

*Percentages may not total 100 because of rounding.

pate, and 22% were not completed for other reasons (eg, not a residential telephone). Of the 4078 willing respondents, 27 who did not know whether they experienced a cold during the past 12 months were removed from the sample population, leaving 4051 adult respondents. These 4051 respondents (2006 men and 2045 women) provided additional data for 2247 children. Age, race, and income distributions of the respondents are shown in **Table 1**.

Survey results are summarized in **Table 2**. The respondents revealed that more than 67% of adults and 87% of children experienced at least 1 non–influenza-related VRTI episode in the past year (weighted average, 72.3%). Of those subjects experiencing at least 1 episode annually, the average adult experienced 2.2 episodes per year, while children younger than 18 years experienced an average of 3.0 episodes annually (weighted average, 2.5 episodes per year). Extrapolating these results to the general population, using the 2000 US Census figures, yields an estimated 500 million episodes annually.

NON–INFLUENZA-RELATED VRTI ASSOCIATED HEALTH CARE USE

Survey respondents reported that adults seek medical attention at a physician's office in 16.1% of the symptomatic episodes, while children visited their physician 31.7% of the time (weighted average, 22.0%). In addition, those with colds or their caregivers contacted their physician by telephone in 4.6% of cases. By applying these use rates to the annual number of episodes previously reported, there are 110 million physician visits and 23.2 million physician telephone calls in the United States yearly. Similarly, an estimated 6 million emergency department visits for the cold occur annually.

Survey respondents reported that more than two thirds (69%) of those with colds self-medicate with an OTC product. Survey respondents experiencing a symptomatic VRTI episode indicated that they receive prescriptions for antibiotics and symptomatic therapies 8.2% and 3.0% of the time, respectively, leading to more than 41 and 15 million prescriptions annually, respectively.

EXPENDITURES

When the survey responses and applicable unit cost estimates (Table 1) were extrapolated to the US population, the estimated total cost in the United States approaches $40 billion annually (95% confidence interval, $31.2-$48.0 billion). Direct medical costs represent about 45% ($17 billion) of the total, and indirect costs represent about 55% ($22.5 billion) of the total costs. Indirect costs can be further divided by whether the illness itself or caring for a sick child was the cause of work loss (**Figure 2**).

Direct Expenditures

Of the $17 billion in direct medical costs for non–influenza-related VRTI episodes, $7.7 billion (45%) is spent on physician services (not including telephone consultations) and $4.8 billion (28%) is spent on individuals whose non–influenza-related VRTI is complicated by acute sinusitis, otitis media, and lower respiratory tract infections (asthma exacerbations were not included). Americans spend $2.9 billion annually on OTC medications and $400 million annually on drugs prescribed for symptomatic relief. In addition, more than $1.1 billion is spent annually on the estimated 41 million unnecessary antibiotic prescriptions for persons experiencing a non–influenza-related VRTI episode.

Indirect Expenditures

An estimated 189 million school days (an average of nearly 1 day per episode) are missed annually as a result of a non–influenza-related VRTI episode.[9] Recall that the calculations included only the proportion of those days associated with the children who live in a 2-parent family with both parents fully employed and those living in a single-parent household in which that parent is fully employed (68% of all family households).[37] In these families, it was assumed that a day of work is missed for each day of school missed. Based on this estimate, 126 million workdays are missed by parents caring for their child. Thus, the indirect costs associated with these missed workdays were estimated to be $14.5 billion annually.

In addition to missed workdays for caregivers, an additional 70 million workdays are missed annually because of employees experiencing a non–influenza-related VRTI episode (an average of 1 day per 4.4 episodes). This translates into an indirect cost of $8.0 billion annually. This estimate does not include costs incurred by those who do not work outside the home, the value of lost leisure time, and decreased productivity while at work (presenteeism).

SENSITIVITY ANALYSIS

The effects of varying individual inputs on the total cost of VRTI-related illness were evaluated using a univariate sensitivity analysis (**Figure 3**). As shown in the fig-

Table 2. Inputs Used to Estimate the Economic Burden of Non–Influenza-Related VRTI

	Weighted Average Estimate per Episode*		
Category	Utilization	Cost, US $	Source
Epidemiological findings			
US population	281 421 906	NA	2000 US Census
Incidence rate of VRTI	72.3% (71.1%-73.5%)	NA	Epidemiological survey
Episodes in people experiencing VRTI/y	2.48 (1.65-3.30)	NA	Epidemiological survey
Total episodes/y	503 528 989 (337 882 694-669 175 284)	NA	Data not available
Direct medical costs			
OTC use	69.1% (67.7%-70.5%)	8.31 (5.58-11.04)	Epidemiological survey
Physician encounter			
Telephone consultation	4.61% (3.96%-5.24%)	0	Epidemiological survey
Office consultation	22.0% (20.2%-23.8%)	57.84 (38.81-76.87)	Epidemiological survey, Mainous et al,[35] and the 1997 MEPS[38]
ED consultation	1.2% (0.7%-1.6%)	211.92 (147.88-292.86)	Mainous et al[35] and the 1997 MEPS[38]
Antibiotic Rx	8.2% (7.4%-9.0%)	26.44 (18.44-36.54)	Epidemiological survey and Cardinale[36]
Symptomatic Rx	3.1% (2.5%-3.6%)	25.13 (16.53-33.73)	Epidemiological survey and Cardinale[36]
Complications			
Sinusitis	0.5% (0.06%-0.32%)	56.78 (39.62-78.48)	Dingle et al[15] and the 1997 MEPS[38]
Otitis media	2.0% (1.3%-2.8%)	66.73 (46.57-92.23)	Dingle et al[15] and the 1997 MEPS[38]
LRTI	3.4% (2.7%-4.2%)	222.06 (154.95-306.87)	Clinical trials and the 1997 MEPS[38]
Indirect costs			
Caregiver			
Missed school days	186 million (NA)	NA	1996 NHIS report[9]
Missed workdays	126 (85-168) million	14.35 (9.63-19.07)†	1996 NHIS report[9] and epidemiological survey
Employee			
Missed workdays	70 (47-93) million	14.35 (9.63-19.07)†	1996 NHIS report,[9] epidemiological survey, and McIsaac et al[39]

Abbreviations: VRTI, viral respiratory tract infection; OTC, over-the-counter; MEPS, Medical Expenditure Panel Survey; ED, emergency department; Rx, prescription; LRTI, lower respiratory tract infection; NHIS, National Health Interview Survey; NA, data not applicable.

*Weighted across adults and children. Data in parentheses are 95% confidence intervals.

†Per hour.

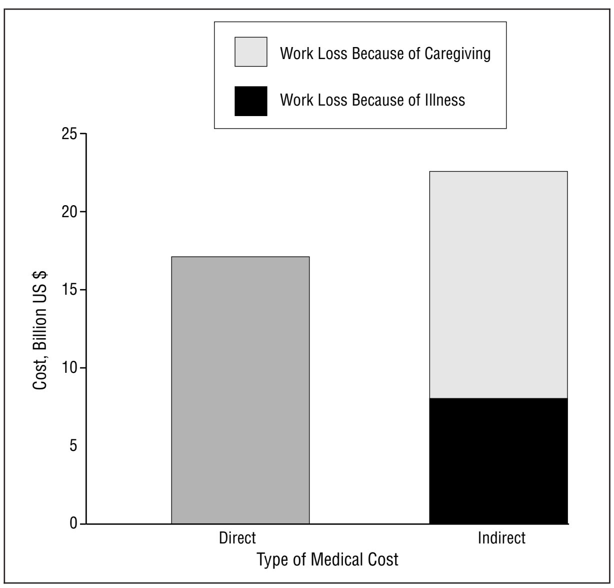

Figure 2. Economic impact of non–influenza-related viral respiratory tract infection, by type of medical cost and type of work loss.

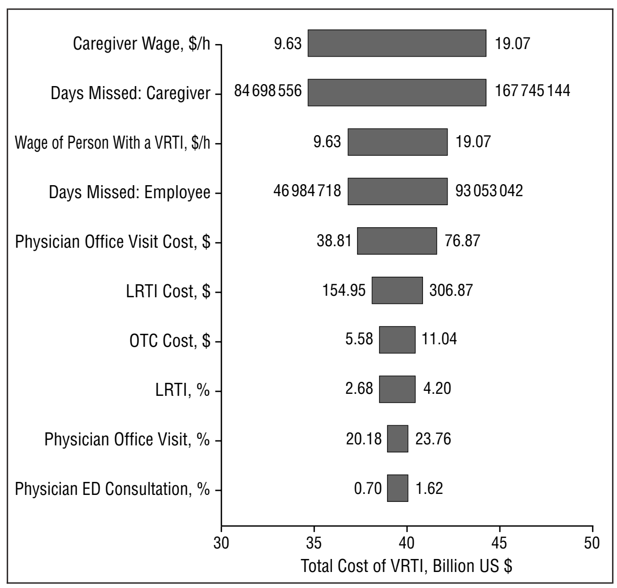

Figure 3. Univariate sensitivity analysis: impact of individual variables on the cost of viral respiratory tract infection (VRTI). The impact of changing the value of selected variables on the total cost of VRTI is shown. Ranges evaluated for individual variables are shown at the ends of the horizontal bars. LRTI indicates lower respiratory tract infection; OTC, over-the-counter; and ED, emergency department.

ure, the variables on which the precision of the total cost of VRTI is most dependent include the hourly wage of the caregiver and the number of workdays missed by caregivers and those with a non–influenza-related VRTI. If the hourly wage for lost productivity was reduced from $14.35 to $9.63 and all other inputs remained constant, the total cost of illness estimate would decrease to $34.7 billion. Likewise, if the caregiver wage was assumed to be $19.07 (a 33% increase), the total cost would be $44.2 billion.

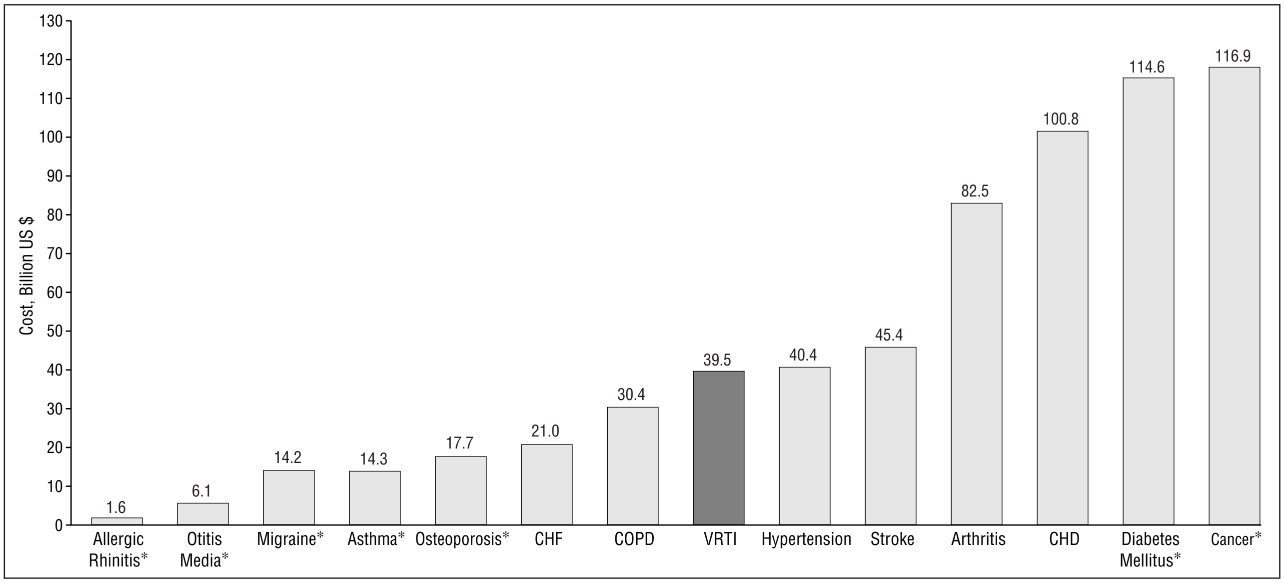

Figure 4. Cost of illness for selected diseases in the United States.[41-48] The asterisk indicates that costs were adjusted to the year 2001, assuming an annual inflation rate of 4%. CHF indicates congestive heart failure; COPD, chronic obstructive pulmonary disease; VRTI, viral respiratory tract infection; and CHD, coronary heart disease.

There were no circumstances in the Monte Carlo simulation or the univariate sensitivity analysis in which the estimated total economic burden of VRTI decreased below $30 billion per year.

COMMENT

Non–influenza-related VRTI has typically been perceived as a self-limiting condition with little or no economic impact on society and the health care system.[21,40] However, our findings suggest that the resultant clinical and cost ramifications attributable to this common condition impose a significant clinical and economic burden on society, approaching or surpassing the costs of many common diseases (**Figure 4**). Our $40 billion estimate places VRTI at or above many significant chronic conditions, including hypertension, chronic obstructive pulmonary disease, congestive heart failure, asthma, and migraine, for total annual cost in the United States (Figure 4). The total cost of VRTI is much greater compared with other acute conditions, such as allergic rhinitis.

Given these findings and that antiviral therapies are forthcoming, this common and expensive disease warrants increased attention from clinicians and policy makers. Based on our results, an innovation that can decrease the number of workdays lost, reduce inappropriate antibiotic use, prevent costly complications, diminish physician visits, or reduce viral transmission will likely have a profound effect on the economic burden.

The burden of non–influenza-related VRTI is highly dependent, not surprisingly, on the incidence. Although the published literature[9,49] reports a wide variability in the range of VRTI incidence, VRTI due to picornavirus—unlike influenza—remains highly prevalent from one year to the next. The National Institute of Allergy and Infectious Disease estimates that the number of colds exceeds 1 billion annually, while the NCHS estimated in 1996 that almost 62 million cases of non–influenza-related VRTI (more specifically, the common cold) required medical attention and resulted in restricted activity.[5,8,9] The National Institute of Allergy and Infectious Disease estimate is based on research[5,15,50] indicating that adults experience 2 to 4 non–influenza-related VRTI cases per year and children experience 6 to 8 cases per year. This estimate may not be representative of the US population because of study sample characteristics. Likewise, the NCHS figure is not representative of the overall incidence because cases were only reported if the respondent sought medical attention or had normal activities restricted, indicating a more severe episode. Our survey-based estimate is intermediate among the published values.

If we were to apply the non–influenza-related VRTI incidence estimate from the NCHS to our conceptual framework and self-reported treatment patterns derived from more than 4000 respondents, the total cost estimate would decrease to roughly $5 billion. Likewise, if we were to assume 1 billion episodes, as cited by the National Institute of Allergy and Infectious Disease, the total annual cost of VRTI would approach $80 billion. Our incidence estimate (500 million annual episodes), derived from a representative national sample, provides a reasonable basis for an estimate of the economic burden of VRTI.

Non–influenza-related VRTI should no longer be viewed as a benign self-limited condition treated exclusively with OTC medications. Primary care office visits (>116 million per year) result in a $7.7 billion cost to the health care system. The survey results indicated that 17% of adults and 33% of children who experience a non–influenza-related VRTI episode seek medical attention through either a physician's office or an emergency department. These figures are similar to those generated from previously conducted epidemiological research.[38]

In addition to the cost of these visits, VRTIs often lead to inappropriate treatment with antibiotics. Our respondents reported that 39% of adults and 33% of children seeking medical attention for non–influenza-related VRTI receive an antibiotic prescription. These findings are concordant with published studies[35,51,52] reporting that 44% and 60% of children and adults, respectively, diagnosed as having non–influenza-related VRTI receive antibiotics. Not only does this behavior result in unnecessary costs but it contributes to the development of antibiotic resistance, a significant public health concern.[53]

The unclear relationship between colds and attributable complications has implications on aggregate cost estimates. We estimate that $4.8 billion is spent annually treating acute sinusitis, otitis media, and lower respiratory tract infections secondary to non–influenza-related VRTI. This estimate is conservative because data were not available to estimate the incremental cost of an asthma or chronic obstructive pulmonary disease exacerbation precipitated by a VRTI episode, despite the fact that non–influenza-related VRTI has been implicated as a major contributor to asthma exacerbations, especially in children.[27,29] In fact, an estimated 45% to 85% of exacerbations in children are thought to be related to VRTIs.[26,28,30,31] In adults, between 10% and 36% of exacerbations are thought to involve VRTI, depending on severity.[28,32] Ongoing research will better establish the link between non–influenza-related VRTI and its bacterial sequelae; from this, a more accurate, and likely higher, cost estimate of attributable complications can be made.

One factor contributing to the lack of attention to VRTI is the lack of effective treatments. Symptomatic remedies of varying effectiveness (available OTC and by prescription), including antihistamines, decongestants, antitussives, analgesics, and alternative or complementary preparations, are available. While these treatment options may reduce the severity of certain symptoms, none treat the underlying cause. There are at least 5 treatments under development that target the most common viruses implicated in non–influenza-related VRTI, including 3 virus capsid–binding agents: pleconaril, pirodavir, and tremacamra. Such treatments may soon offer physicians the first therapeutic alternative to actually diminish viral load.

The methods and inputs used in the estimation of the economic burden of VRTI are subject to some important limitations. First, our survey method is subject to respondent recall bias. To minimize the effect of subject recall, a sensitivity analysis was performed to assess how each input variable affected the final aggregate economic estimates.

Second, while our objective was to capture the complete costs of non–influenza-related VRTI, data limitations prevented the inclusion of several important variables, including costs of telephone calls to physicians, costs attributable to VRTI-associated asthma and acute exacerbations of chronic bronchitis, and reduced productivity at work while ill. It is most likely that inclusion of these inputs would further increase the aggregate cost estimates presented.

Third, the data used to estimate the frequency of lower respiratory complications resulting from a non–influenza-related VRTI episode were obtained from the placebo groups of controlled clinical trials conducted in otherwise healthy individuals. Thus, the base-case model underestimates the frequency of such complications in high-risk groups, such as elderly persons, children, and immunocompromised hosts. This limitation likely generates a conservative cost estimate.

Fourth, the effects of viral illness in the workplace were not fully evaluated. Specifically, the effect of viral illness on productivity while at work and transmission to others is critical in setting employer-based policies, such as implementing educational and disease management initiatives. Because most viral transmission occurs among preschool- and school-aged children and their family members, an intervention that slowed transmission would yield substantial benefits.[54]

Fifth, although we took an analytical approach to exclude symptomatic episodes due to influenza, there remains a possibility—despite these best efforts—that some of these self-reported symptomatic episodes were in fact caused by influenza. This limitation is tempered by the fact that influenza accounts for only 9% of total upper respiratory tract illnesses and 13% of upper respiratory tract illnesses that lead to physician consultation.[5] Thus, even if all influenza episodes (an extremely unlikely event) in a respondent were included, our cost estimates would not be expected to vary by more than 10%. Further diminishing this concern was that the 2000-2001 influenza season was mild in the United States.[55]

Finally, inputs were derived from studies using various methods and were generated in different years and then extrapolated to the estimated 500 million non–influenza-related VRTI episodes that emerged from our survey. As a result, any biases and error contained in any one input may be further compounded in our estimate. Resultant sensitivity analyses to assess the influence of individual data inputs suggest that the results are relatively robust.

In conclusion, this study presents a rigorous approach to estimate the economic impact of non–influenza-related VRTI, the most common disease in humans. Viral respiratory tract infection not only is important in terms of clinical morbidity but also imposes a significant economic burden to the health care system and to society, greater than many important chronic conditions, including hypertension, chronic obstructive pulmonary disease, and congestive heart failure. Hence, when it comes to burden of illness, there is nothing common about the common cold. While this study provides a preliminary estimate, future research is needed to more precisely quantify the economic burden of VRTI.

As antiviral treatments become available, an improved understanding of the effect of these therapies on the clinical and economic outcomes of non–influenza-related VRTI will guide decision makers in their assessment of these innovative therapies and ultimately influence access to them.

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REFERENCES

1. Denny FW Jr. The clinical impact of human respiratory virus infections. *Am J Respir Crit Care Med*. 1995;152(suppl, pt 2):S4-S12.
2. Fahey T, Stocks N, Toby T. Systematic review of the treatment of upper respiratory tract infection. *Arch Dis Child*. 1998;79:225-230.
3. Monto AS, Bryan ER, Ohmit S. Rhinovirus infections in Tecumseh, Michigan: frequency of illness and number of serotypes. *J Infect Dis*. 1987;156:43-49.
4. Arruda E, Pitkaranta A, Witek TJ Jr, Doyle CA, Hayden FG. Frequency and natural history of rhinovirus infections in adults during autumn. *J Clin Microbiol*. 1997; 35:2864-2868.
5. Monto AS, Sullivan KM. Acute respiratory illness in the community: frequency of illness and the agents involved. *Epidemiol Infect*. 1993;110:145-160.
6. Gwaltney JM, Hendley JO, Simon G, Jordan WS. Rhinovirus infections in an industrial population, II: characteristics of illness and antibody response. *JAMA*. 1967;202:158-163.
7. Monto AS. Viral respiratory infections in the community: epidemiology, agents, and interventions. *Am J Med*. 1995;99(suppl 6B):25S-27S.
8. Turner RB. The common cold. *Pediatr Ann*. 1998;27:790-795.
9. Adams PF, Hendershot GE, Marano MA. Current estimates from the National Health Interview Survey, 1996. *Vital Health Stat 10*. 1999;No. 200:59, 66.
10. Nicholson KG, Kent J, Hammersley V, Cancio E. Acute viral infections of upper respiratory tract in elderly people living in the community: comparative, prospective, population based study of disease burden. *BMJ*. 1997;315:1060-1064.
11. Wald TG, Shult P, Krause P, Miller BA, Drinka P, Gravenstein S. A rhinovirus outbreak among residents of a long-term care facility. *Ann Intern Med*. 1995;123: 588-593.
12. McIntosh K, Halonen P, Ruuskanen O. Report of a workshop on respiratory viral infections: epidemiology, diagnosis, treatment, and prevention. *Clin Infect Dis*. 1993;16:151-164.
13. Patel JA, Reisner B, Vizirinia N, Owen M, Chonmaitree T, Howie V. Bacteriologic failure of amoxicillin-clavulanate in treatment of acute otitis media caused by nontypeable *Haemophilus influenzae*. *J Pediatr*. 1995;126(5 pt 1):799-806.
14. Sung BS, Chonmaitree T, Broemeling LD, et al. Association of rhinovirus infection with poor bacteriologic outcome of bacterial-viral otitis media. *Clin Infect Dis*. 1993;17:38-42.
15. Dingle JH, Badger GF, Jordan WS Jr. *Illness in the Home: Study of 25,000 Illnesses in a Group of Cleveland Families*. Cleveland, Ohio: Press of Western Reserve University; 1964:1.
16. Pitkaranta A, Arruda E, Malmberg H, Hayden F. Detection of rhinovirus by reverse transcription PCR of sinus brushings in patients with acute community acquired sinusitis. *J Clin Microbiol*. 1997;35:1791-1793.
17. Turner BW, Cail WS, Hendley JO, et al. Physiologic abnormalities in the paranasal sinuses during experimental rhinovirus colds. *J Allergy Clin Immunol*. 1992; 90:474-478.
18. Gwaltney JM Jr, Phillips CD, Miller RD, Riker DK. Computed tomographic study of the common cold. *N Engl J Med*. 1994;330:25-30.
19. Chidekel AS, Rosen CL, Bazzy AR. Rhinovirus infection associated with serious lower respiratory illness in patients with bronchopulmonary dysplasia. *Pediatr Infect Dis J*. 1997;16:43-47.
20. Collinson J, Nicholson KG, Cancio E, et al. Effects of upper respiratory infections in patients with cystic fibrosis. *Thorax*. 1996;51:1115-1122.
21. Couch RB, Englund JA. Respiratory viral infections in immunocompetent and immunocompromised persons. *Am J Med*. 1997;102(suppl 1):2-9.
22. Rabella N, Rodriguez P, Labeaga R, et al. Conventional respiratory viruses recovered from immunocompromised patients: clinical considerations. *Clin Infect Dis*. 1999;28:1043-1048.
23. Whimbey E, Champlin RE, Couch RB, et al. Community respiratory virus infections among hospitalized adult bone marrow transplant recipients. *Clin Infect Dis*. 1996;22:778-782.
24. Ghosh S, Champlin R, Couch R, et al. Rhinovirus infections in myelosuppressed adult blood and marrow transplant recipients: trivial or fatal? Paper presented at: The 8th International Congress on Infectious Disease; May 15-18, 1998; Boston, Mass.
25. Whimbey E, Englund JA, Couch RB. Community respiratory virus infections in immunocompromised patients with cancer. *Am J Med*. 1997;102(suppl 1):10-18.
26. Pitkaranta A, Hayden FG. Rhinoviruses: important respiratory pathogens. *Ann Med*. 1998;30:529-537.
27. Minor TE, Baker JW, Dick EC, et al. Greater frequency of viral respiratory infections in asthmatic children as compared with their nonasthmatic siblings. *J Pediatr*. 1974;85:472-477.
28. Teichtahl H, Buckmaster N, Pertnikovs E. The incidence of respiratory tract infection in adults requiring hospitalization for asthma. *Chest*. 1997;112:591-596.
29. Minor TE, Dick EC, DeMeo AN, Ouellette JJ, Cohen M, Reed CE. Viruses as precipitants of asthmatic attacks in children. *JAMA*. 1974;227:292-298.
30. Rakes GP, Eurico A, Ingram JM, et al. Rhinovirus and respiratory syncytial virus in wheezing children requiring emergency care. *Am J Respir Crit Care Med*. 1999; 159:785-790.
31. Johnston SL, Pattemore PK, Sanderson G, et al. Community study of role of viral infections in exacerbations of asthma in 9-11 year old children. *BMJ*. 1995; 310:1225-1229.
32. Beasley R, Coleman ED, Hermon Y, Holst PE, O'Donnell TV, Tobias M. Viral respiratory tract infection and exacerbations of asthma in adult patients. *Thorax*. 1988;43:679-683.
33. Nicholson KG, Kent J, Ireland DC. Respiratory viruses and exacerbations of asthma in adults. *BMJ*. 1993;307:982-986.
34. Hayden FG, Kim K, Hudson S. Pleconaril treatment reduces duration and severity of viral respiratory infection (common cold) due to picornaviruses. Paper presented at: the 41st Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC); December 16-19, 2001; Chicago, Ill.
35. Mainous AG III, Hueston WJ, Clark JR. Antibiotics and upper respiratory infection: do some folks think there is a cure for the common cold? *J Fam Pract*. 1996; 42:357-361.
36. Cardinale V, ed. *Drug Topics Red Book*. Montvale, NJ: Medical Economics Books; 2001.
37. Bureau of Labor Statistics. Labor force statistics from the current population survey. Available at: http://www.bls.gov/home.htm. Accessed June 7, 2001.
38. Agency for Healthcare Research and Quality. Introduction to MEPS data & publications. Available at: http://www.meps.ahrq.gov/data_public.htm. Accessed February 1, 2001.
39. McIsaac WJ, Levine N, Goel V. Visits by adults to family physicians for the common cold. *J Fam Pract*. 1998;47:366-369.
40. Lorber B. The common cold. *J Gen Intern Med*. 1996;11:229-236.
41. Malone DC, Lawson KA, Smith DH, Arrighi MH, Battista C. A cost of illness study of allergic rhinitis in the United States. *J Allergy Clin Immunol*. 1997;99(pt 1):22-27.
42. Gates GA. Cost-effectiveness considerations in otitis media treatment. *Otolaryngol Head Neck Surg*. 1996;114:525-530.
43. Wiess KB, Gergen PJ, Hodgson TA. An economic evaluation of asthma in the United States.. *N Engl J Med*. 1992;326:862-866.
44. National Osteoporosis Foundation. New study finds cost of treating osteoporosis significantly underestimated [press release]. Available at: http://www.nof.org/news/. Accessed September 24, 2001.
45. Hu HX, Markson LE, Lipton RB, Stewart WF, Berger ML. Burden of migraine in the United States: disability and economic costs. *Arch Intern Med*. 1999;159: 813-818.
46. American Heart Association. *2001 Heart and Stroke Statistical Update*. Dallas, Tex: American Heart Association; 2000.
47. American Lung Association. American Lung Association fact sheet: chronic obstructive pulmonary disease (COPD). Available at: http://www.lungusa.org/diseases/copd_factsheet.html. Accessed September 24, 2001.
48. Varmus H. *Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support*. Bethesda, Md: Office of the Director, National Institutes of Health, Dept of Health and Human Services; 1997.
49. Monto AS, Cavallero JJ. The Tecumseh study of respiratory illness, II: patterns of occurrence of infection with respiratory pathogens, 1965-1969. *Am J Epidemiol*. 1971;94:280-289.
50. Monto AS, Ullman BM. Acute respiratory illness in an American community: the Tecumseh study. *JAMA*. 1974;227:164-169.
51. Nyquist A, Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. *JAMA*. 1998;279: 875-877.
52. Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA*. 1997; 278:901-904.
53. Fendrick AM, Saint S, Brook I, Jacobs MR, Pelton S, Sethi S. Diagnosis and treatment of upper respiratory tract infections in the primary care setting. *Clin Ther*. 2001;23:1683-1706.
54. Hendley JO, Gwaltney JM Jr, Jordan WS Jr. Rhinovirus infections in an industrial population, IV: infections within families of employees during two fall peaks of respiratory illness. *Am J Epidemiol*. 1969;89:184-196.
55. Update: influenza activity—United States and worldwide, 2000-01 season, and composition of the 2001-02 influenza vaccine. *MMWR Morb Mortal Wkly Rep*. 2001;50:466-479.