CLINICAL THERAPEUTICS®/VOL. 21, NO. 4, 1999

Impact of Palivizumab on Expected Costs of Respiratory Syncytial Virus Infection in Preterm Infants: Potential for Savings

Albert Marchetti, MD, Helen Lau, MS, Raf Magar, Liping Wang, MS, and Giovanna Devercelli, MBA

Health Economics Research, Secaucus, New Jersey

ABSTRACT

In its clinical assessment of the respiratory syncytial virus (RSV)–specific monoclonal antibody palivizumab, the IMpact-RSV Study Group demonstrated a reduction in hospitalizations for RSV-related lower respiratory tract infection in infants who received prophylaxis compared with infants who did not receive prophylaxis. An assessment of the RSV-related expenses for managing both groups of infants is needed to provide insight into the value of prophylaxis. The present study was conducted to identify and compare RSV-related health care expenditures incurred by infants who did not receive prophylaxis throughout one RSV season and after. Using a decision-analytic model populated with data from the contemporary medical literature, a pharmacoeconomic study was conducted from the perspective of the payer. Probabilities for RSV-related hospitalizations of infants who did and did not receive prophylaxis were abstracted from several published studies. Components of inpatient and outpatient care were identified through examination of hospital records, reviews of the published literature, and consultation with expert clinicians. Charges related to prophylaxis and medical management of infection were abstracted from hospital billing records and published data. Appropriate charges were applied to decision-tree branches and multiplied by in-line probabilities for outcomes. Products at terminal nodes were summed to establish total expected charges for both groups of infants. Widespread clinical use of prophylactic palivizumab would result in incremental expenses ≤$3459 per infant or cost savings ≤$39,107 per infant. The variability in value of prophylaxis derives from the rate of RSV-related hospitalizations in the community and the total health care expense of managing infected infants.

Key words: respiratory syncytial virus, palivizumab, cost benefit, prophylaxis.

Accepted for publication March 31, 1999.

0149-2918/99/$19.00

INTRODUCTION

Clinical decisions in medicine are no longer made on the basis of safety and efficacy alone. Today, the cost of care also influences the selection of health care interventions, as payers and providers seek to match available funds with desired resources. Although patient welfare should always be at the heart of clinical decisions, individual needs must be weighed against societal concerns and overall ability to pay for the broad range of products and services demanded by diverse sectors of society. To optimize clinical and economic outcomes, care must be efficient and cost-beneficial; that is, health care professionals must provide only the most effective services that produce the greatest impact at the least cost and on such a scale that incremental expenses are justified by incremental benefits.[1]

In considering respiratory syncytial virus (RSV) infection of infants and prophylaxis with the RSV-specific monoclonal antibody palivizumab,* the cost of protection must be compared with the cost of infection. Direct medical expenditures, such as the cost of palivizumab and related expenses of preventing lower respiratory tract infection, as well as the human and material resources (inpatient and outpatient components of care) consumed during the treatment of infected infants must be part of the assessment. In addition, there are substantial indirect medical costs, various nonmedical costs (eg, loss of productivity and wages, and prevention of infectious spread of RSV), and intangible costs (emotional impact on parents and families of infected children) to be considered. Such factors have an impact on the total societal cost of RSV infection and prophylaxis.

Unfortunately, accurate appraisal of the economic consequences of RSV infection (burden of illness) and the value of prophylaxis have been confounded by numerous factors. First, epidemiologic data are poorly characterized and incompletely reported. Incidence rates vary greatly according to differences in the extent of RSV testing to establish the cause of infection, regional/seasonal severity,[2–4] virulence of RSV strain and subspecies,[5–7] quality of neonatal care between institutions,[8–10] and various socioeconomic factors.[11–13] Moreover, because clinical trial protocols mandate RSV infection control through education, enhanced hygiene, and other precautionary anti-infection measures, attack rates for study infants are likely to be artificially low. Finally, inpatient and outpatient resource utilization and related costs vary greatly by gestational age, birth weight, age at infection, preexisting comorbidities, severity of infection, quality of care, hospitalization rates, rehospitalization rates, and long- and short-term sequelae of infection.

For example, estimated rates of hospitalization for respiratory infections in premature infants range from 41[14] to 85[15] admissions per 100 child-years. As a causative agent, RSV accounts for 42% to 79% of all reported infections[16–18] and 100% of infections assessed in clinical trials.[19–21]

Regardless of the incidence rates for inpatient service, the reported cost per hospitalization among infected infants has also varied widely, from $2025 to $166,375 in a single institution.[22] These charges reflect resource utilization for 1

*Trademark: Synagis™ (MedImmune, Inc., Gaithersburg, Maryland).

hospital stay and include expenses for personnel, intensive care, ventilation, oxygen, specialized respiratory therapy, medications, and other medical services. The expense of the subsequent ambulatory and/or institutional care that is required by many infants in the 6 to 12 months after the initial RSV hospitalization and the charges for outpatient services dedicated to the treatment of nonhospitalized RSV-infected infants are not included in such calculations. Thus costs of a single hospital stay may substantially underestimate the full financial impact of infection.

Likewise, the lifelong cost of managing patients with reactive respiratory disease, one of the suggested but not established long-term sequelae of early RSV infection,[23–28] has not yet been determined or factored in to economic analyses. Moreover, most indirect and intangible costs have generally been overlooked. Although they may be substantial for the parents and families of affected infants, they do not have a direct impact on health care budgets and are not normally considered by payers or providers.

To address these and other pressing issues related to cost and value, health economic studies have emerged as important tools in the assessment of clinical and economic consequences of health care products and services. Comparison of costs between interventions and their alternatives reveals cost savings or incremental spending. In terms of RSV infection and prophylaxis, there are 2 important economic questions: (1) Is the cost of providing prophylaxis to the universe of infants at risk for RSV infection greater or less than the cost of treating all infants who become infected? and (2) If incremental costs are incurred with prophylaxis, are they balanced by incremental benefits?

Previously reported clinical and economic assessments relating to RSV treatment, prophylaxis, and infection are summarized in the following paragraphs. A pharmacologic review[29] showed that prophylaxis with RSV intravenous immune globulin (IVIG) and therapy with ribavirin constituted a cost-effective strategy for preventing and treating RSV infections. A prospective 2-year study[30] of respiratory rehospitalization rates for premature infants (<32 weeks of gestation) revealed a 36% rehospitalization rate for respiratory illnesses following initial hospital discharge, with a similar rehospitalization rate of 2.5% observed among matched full-term infants.

An analysis of resources consumed by preterm infants after initial hospital discharge[14] indicated that approximately 55% of preterm infants were readmitted with respiratory infections. Compared with healthy control subjects, these infants required more mean hospital days (48 days vs 2 days) and neonatal intensive care (100% vs 4%). Moreover, 80% required ventilation, and 15% were still oxygen dependent at 28 days of age.

A cost-effectiveness analysis of prophylaxis with RSV IVIG[31] indicated that the cost per life-year saved was $24,305, which the authors of the analysis considered to be cost-effective compared with other health care interventions. An economic evaluation of RSV infection in Canadian children ≤4 years of age[32] showed that cost savings could best be achieved by preventing hospitalization or reducing hospital length of stay.

An economic assessment of viral respiratory disease in specialized patient populations[33] revealed that RSV prophylaxis could lead to potential cost savings. A cost-benefit study of RSV prophylaxis in

preterm infants and infants with bronchopulmonary dysplasia[34] revealed incremental spending with prophylaxis.

A number-needed-to-treat analysis based on clinical trial data concerning hospitalization rates with RSV IVIG prophylaxis[35] indicated that 16 infants must receive prophylaxis to prevent 1 hospitalization. A prospective cohort study of the hospital readmission rate among preterm infants[15] documented 91 respiratory-related rehospitalizations per 100 children in the first year of life. A cost-benefit analysis in high-risk infants[22] demonstrated that RSV IVIG prophylaxis is cost-effective in infants with bronchopulmonary dysplasia.

The objective of the present study was to identify and compare expected RSV-related health care expenditures incurred by preterm infants who received prophylaxis with palivizumab versus preterm infants who did not receive such prophylaxis.

MATERIALS AND METHODS

A pharmacoeconomic study was conducted from the payer's perspective using a decision tree populated with data from the current medical literature (Figure 1). For infants at risk for RSV infection, the tree depicts 2 clinical options (prophylaxis with palivizumab or no prophylaxis); shows the clinical consequences of each

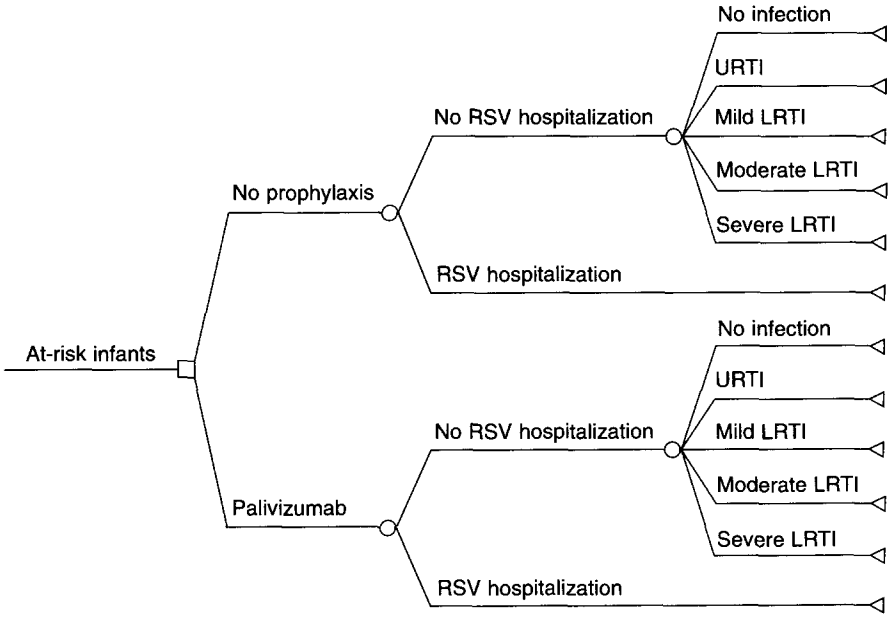

Figure 1. Decision analytic model showing management options and their clinical consequences in preterm infants who did and did not receive prophylaxis with palivizumab for respiratory syncytial virus (RSV) infection, based on data from the IMpact trial.[20] URTI = upper respiratory tract infection; LRTI = lower respiratory tract infection.

Table I. Description of respiratory scores from the IMpact study,[20] adapted from Groothuis et al.[19]

Score	Description
0	No upper or lower respiratory tract infection
1	Upper respiratory tract infection
2	Mild lower respiratory tract infection
3	Moderate lower respiratory tract infection
4	Severe lower respiratory tract infection
5	Mechanically ventilated

decision; and details the clinical pathways and resources required for infants undergoing prophylaxis or treatment for RSV infection. The decision tree also serves as the foundation for estimating the anticipated charges related to each option. It is based predominantly on the IMpact clinical trial,[20] which assessed the safety and efficacy of palivizumab in preventing hospitalizations due to RSV infection in preterm infants, including those with bronchopulmonary dysplasia.

Outcome Measures

Outcome measures define the clinical consequences of health care interventions. Some measures are general (eg, life-years gained, disease-free days) and have widespread applicability. Others are specific to the research for which they were developed. Given its overall impact on the study results, the selected measure must be relevant to the chosen research perspective. In the present analysis, the most influential outcome measure was the rate of RSV hospitalizations of infants who did and did not receive prophylaxis. This was defined as the likelihood of hospitalization after RSV infection and expressed as a probability ranging from 0 to 1.

Another significant factor in the present economic assessment was the need for and level of outpatient care required to manage RSV-infected infants who did not require hospitalization. In the decision tree, the intensity of and related charges for short-term (RSV season only) outpatient care are stratified by severity of infection from the IMpact study,[20] based on respiratory scores adapted from Groothuis et al[19] (Table I). A respiratory score is the mode of 3 component scores based on oxygen saturation, respiratory rate, and severity of pulmonary function (ie, retractions, wheezing, and crackles) compared with baseline values for usual oxygen flow. In the absence of a mode, a mean score is used to determine the infant's respiratory score.

The IMpact Trial

The IMpact clinical trial[20] was a randomized, double-masked, placebo-controlled, international study conducted during the 1996 to 1997 RSV season. It demonstrated that palivizumab was safe and effective in the prevention of RSV-related hospitalizations of at-risk infants. A total of 1502 premature infants (≤35 weeks of gestation) with or without bronchopulmonary dysplasia were randomized to receive 5 intramuscular injections of either palivizumab or placebo every 30 days from November/December 1996 through March/April 1997. Patient groups were balanced at entry for demographic characteristics and RSV risk factors.

The primary end point of the study was hospitalization with confirmed RSV infection. Other data elements included total length of stay, time spent in intensive

care, time spent on supplemental oxygen, time spent on mechanical ventilation, and total days with moderate or severe lower respiratory tract illness. The IMpact-RSV Study Group observed a 55% reduction in RSV-related hospitalizations in the palivizumab group compared with the placebo group (95% confidence interval, 38% to 72%). Moreover, infants who received prophylaxis had proportionally fewer total RSV hospital days, time on supplemental oxygen, and hospital days with moderate or severe lower respiratory tract illness. No significant differences in adverse events were observed between infants who received prophylaxis and those who received placebo.

Data Sources

The present analysis included data on RSV-related hospitalizations of infants who did not receive prophylaxis but shared similar demographic characteristics and RSV risk factors with infants who did receive prophylaxis in the IMpact trial. These data were derived from the PREVENT[21] and National Institute of Allergy and Infectious Diseases (NIAID)—Respiratory Syncytial Virus Immune Globulin[19] studies, which were conducted during the 1994/1995 and 1989–1992 RSV seasons, respectively. Relevant data included RSV-related hospitalization rates and the previously discussed secondary end points associated with hospital stay.

When individual hospital rates from the 3 clinical trials—IMpact, PREVENT, and NIAID—were combined to broaden and improve the data for infants who did not receive prophylaxis, the weighted combined hospitalization rate was 12.3%. The hospitalization rate for infants who received prophylaxis with palivizumab was 4.8% (IMpact trial), representing a 61% reduction compared with the combined rate for all infants enrolled in the clinical trials who did not receive prophylaxis. Based on our interpretations, other studies have estimated hospitalization rates for preterm infants who did not receive prophylaxis at 10.6%,[20] 13.5%,[21] 20.7%,[14] 22.4%,[19] 36.1%,[30] and 42.6%.[15]

Additionally, we identified components of inpatient and outpatient care required in the treatment of RSV infection by examining hospital records, conducting reviews of the published literature, and consulting with expert clinicians. Searches of Dialog, PubMed, Medscape, BioMedNet, and other information sources were used to identify articles on the epidemiology of RSV infection, infant respiratory disease, rehospitalizations, prophylaxis, economics, cost of illness, and resource utilization. Experts in the areas of pediatrics, infectious diseases, and pharmacology who had extensive experience in the management of at-risk and RSV-infected infants were recruited to participate in the study as clinical advisors. Advisors were surveyed to identify components of standard care for high-risk infants with RSV infections and to assess the immediate and subsequent sequelae of RSV infection and hospitalization. Advisors were contacted by phone or e-mail to clarify any questions. All advisors were paid an honorarium equivalent to remuneration for continuing medical education programs.

Charges related to prophylaxis with palivizumab and outpatient care were abstracted from public sources.[36–39] Hospital charges for RSV-related admissions, which ranged from $10,236[40] to

Table II. Expected per-patient charges for unprotected high-risk infants.

RSV Hospitalization Rate (%)	Hospitalization Charge ($)					
	10,236[40]	19,190*	27,101[22]	68,067[33]	77,666[32]	166,375[22]
10.60[20]	1116	2065	2904	7246	8264	17,667
12.30*	1290	2391	3364	8403	9584	20,495
13.46[21]	1408	2613	3678	9192	10,484	22,424
20.70[14]	2147	4000	5638	14,118	16,105	34,467
22.41[19]	2321	4328	6100	15,281	17,432	37,312
36.10[30]	3718	6950	9806	24,595	28,060	60,084
42.60[15]	4381	8195	11,565	29,017	33,106	70,896

RSV = respiratory syncytial virus.
*Present analysis.

$166,375[22] (Table II), were culled from previously published reports.[22,32,33,40] The lower figure was based on a multicenter assessment of infants regardless of comorbidities,[40] and the higher figure was based on an assessment of high-risk infants at a single institution.[22]

Calculation of Expected Cost

The decision tree in this study provides the framework for calculating expected RSV-related health care expenditures incurred by infants who did and did not receive prophylaxis. Within the tree, the required components of care for each clinical pathway are identified, along with the associated inpatient and outpatient charges. These expenditures are then weighted by probabilities along each branch to derive expected charges at the terminal nodes, which expected charges are then added to arrive at the total expected charge for the entire tree. The probabilities applied within the decision tree represent the likelihood of necessary inpatient and outpatient care. "Total expected charges" represents the anticipated expense of providing prophylaxis and treating RSV infection in an infant at risk, based on the clinical pathways and therapeutic options depicted on the tree. Charges related to the management of adverse events due to prophylaxis were not included.

Several analyses were performed to determine the economic consequences of 38%, 55%, 61%, and 72% reductions in previously reported hospitalization rates for infants who did not receive prophylaxis[20]; variable hospital charges abstracted from medical records and the published literature; and outpatient expenses stratified by severity of infection. IMpact study results cited statistically insignificant differences in systemic adverse events. Local adverse events were reported in 1.8% of patients not treated with palivizumab prophylaxis versus 2.7% of patients treated with palivizumab. No serious localized events were reported, and all local events (ie, erythema, pain, swelling, and bruising) were mild and of short duration. Based on these findings, charges related to local and

Table III. Expected per-patient charges for protected high-risk infants, based on various reductions in hospitalization rates.

A. 61% Reduction

RSV Hospitalization Rate (%)		Hospitalization Charge ($)					
Unprotected	–61%	10,236[40]	19,190*	27,101[22]	68,067[33]	77,666[32]	166,375[22]
10.60[20]	4.13	4575	4945	5272	6965	7362	11,029
12.30*	4.80	4642	5072	5451	7416	7877	12,132
13.46[21]	5.25	4688	5159	5574	7724	8228	12,885
20.70[14]	8.07	4977	5699	6338	9645	10,420	17,582
22.41[19]	8.74	5045	5827	6519	10,099	10,938	18,691
36.10[30]	14.08	5589	6850	7964	13,731	15,083	27,572
42.60[15]	16.61	5848	7335	8650	15,456	17,051	31,789

B. 55% Reduction

RSV Hospitalization Rate (%)		Hospitalization Charge ($)					
Unprotected	–55%	10,236[40]	19,190*	27,101[22]	68,067[33]	77,666[32]	166,375[22]
10.60[20]	4.77	4640	5067	5444	7398	7856	12,087
12.30*	5.54	4718	5213	5651	7919	8450	13,360
13.46[21]	6.06	4771	5313	5792	8274	8855	14,228
20.70[14]	9.32	5103	5937	6674	10,490	11,384	19,648
22.41[19]	10.08	5182	6085	6882	11,014	11,982	20,928
36.10[30]	16.25	5810	7265	8550	15,205	16,764	31,175
42.60[15]	19.17	6109	7825	9342	17,195	19,035	36,040

RSV = respiratory syncytial virus.
*Present analysis.

(continued)

systemic adverse events were considered inconsequential.

RESULTS

With a 61% palivizumab-related reduction in the RSV hospitalization rate for all infants at risk of lower respiratory tract infection, expected RSV-related expenses per infant who received prophylaxis range from $4575 to $31,789 (Table IIIA), whereas similar expenses for infants who did not receive prophylaxis range from $1116 to $70,896 (Table II), based on per-patient hospital charges. Consequently, widespread clinical use of palivizumab can result in incremental expenses as high as $3459 per infant or cost savings as

Table III. (continued)

C. 72% Reduction

RSV Hospitalization Rate (%)		Hospitalization Charge ($)					
Unprotected	–72%	10,236[40]	19,190*	27,101[22]	68,067[33]	77,666[32]	166,375[22]
10.60[20]	2.97	4456	4722	4956	6172	6457	9090
12.30*	3.44	4504	4813	5085	6496	6827	9882
13.46[21]	3.77	4771	5313	5792	8274	8855	14,228
20.70[14]	5.80	4744	5263	5722	8096	8652	13,794
22.41[19]	6.27	4793	5355	5851	8422	9024	14,591
36.10[30]	10.11	5184	6089	6889	11,030	12,000	20,967
42.60[15]	11.93	5370	6438	7381	12,268	13,413	23,994

D. 38% Reduction

RSV Hospitalization Rate (%)		Hospitalization Charge ($)					
Unprotected	–38%	10,236[40]	19,190*	27,101[22]	68,067[33]	77,666[32]	166,375[22]
10.60[20]	6.57	4823	5412	5932	8624	9255	15,085
12.30*	7.63	4931	5614	6217	9341	10,073	16,838
13.46[21]	8.35	4771	5313	5792	8274	8855	14,228
20.70[14]	12.83	5462	6611	7627	12,884	14,116	25,501
22.41[19]	13.89	5182	6085	6882	11,014	11,982	20,928
36.10[30]	22.38	6436	8440	10,211	19,380	21,528	41,383
42.60[15]	26.41	6847	9212	11,302	22,122	24,657	48,087

RSV = respiratory syncytial virus.
*Present analysis.

great as $39,107 per infant. A 55% reduction in hospitalization rates would change the estimated RSV-related expense range for infants receiving prophylaxis to $4640 to $36,040 (Table IIIB), resulting in incremental expenses as high as $3524 per infant or cost savings as great as $34,856 per infant. Tables IIIC and IIID convey similar information, assuming 72% and 38% reductions in hospitalization rates for all infants at risk. These percentages are based on IMpact trial data and represent upper and lower 95% confidence interval end point estimates.

For specified subgroups of high-risk infants investigated in the IMpact trial, the following reductions in hospitalization rates were observed: 39% (bronchopulmonary dysplasia only); 47% (gestational age <32 weeks); 78% (all infants ≤35 weeks gestational age); 80% (gestational age 32 to 35 weeks); and 82% (gestational

Table IV. Expected per-patient charges for (A) unprotected high-risk infants and (B) protected special high-risk infants.

A. Unprotected High-Risk Infants

	RSV Hospitalization Rate[41] (%)	Hospitalization Charge ($)					
High-Risk Group	Unprotected	10,236[40]	19,190*	27,101[22]	68,067[33]	77,666[32]	166,375[22]
BPD	12.8	1341	2487	3499	8743	9972	21,327
Premature	8.1	861	1587	2227	5546	6323	13,509
<32 weeks	11.0	1157	2142	3012	7519	8574	18,332
32–35 weeks	9.8	1035	1912	2687	6702	7643	16,336
32–35 weeks, no BPD	10.0	1055	1951	2742	6838	7798	16,669

B. Protected Special High-Risk Infants

	RSV Hospitalization Rate[41] (%)	Hospitalization Charge ($)					
High-Risk Group	Protected	10,236[40]	19,190*	27,101[22]	68,067[33]	77,666[32]	166,375[22]
BPD	7.9	4949	5649	6266	9465	10,214	17,141
Premature	1.8	4335	4494	4635	5365	5536	7117
<32 weeks	5.8	4748	5270	5731	8119	8679	13,851
32–35 weeks	2.0	4353	4528	4683	5486	5675	7413
32–35 weeks, no BPD	1.8	4337	4498	4640	5378	5550	7147

RSV = respiratory syncytial virus; BPD = bronchopulmonary dysplasia; premature = ≤35 weeks' gestation.
*Present analysis.

age 32 to 35 weeks, no bronchopulmonary dysplasia).[41] Expected charges for these subgroups of at-risk infants were based exclusively on data from the IMpact trial (Tables IVA and IVB).

Figures 2 and 3 depict "break-even boundary lines" based on RSV hospitalization rates and charges for all high-risk infants (Figure 2) and subgroups of high-risk infants (Figure 3). Based on decision-tree calculations, the total expected charge per hospitalization per infant is a function of RSV hospitalization rates for infants not receiving prophylaxis, palivizumab-related reductions in those rates, and hospital charges per patient. By varying these inputs and plotting values for the expected charge per hospitalization per infant, a "break-even boundary line" between incremental costs for RSV prophylaxis and cost savings associated with palivizumab was charted. Combined probability values and hospital charges that fall above each interface define cost savings associated with prophylaxis; combinations that fall below the boundary do not.

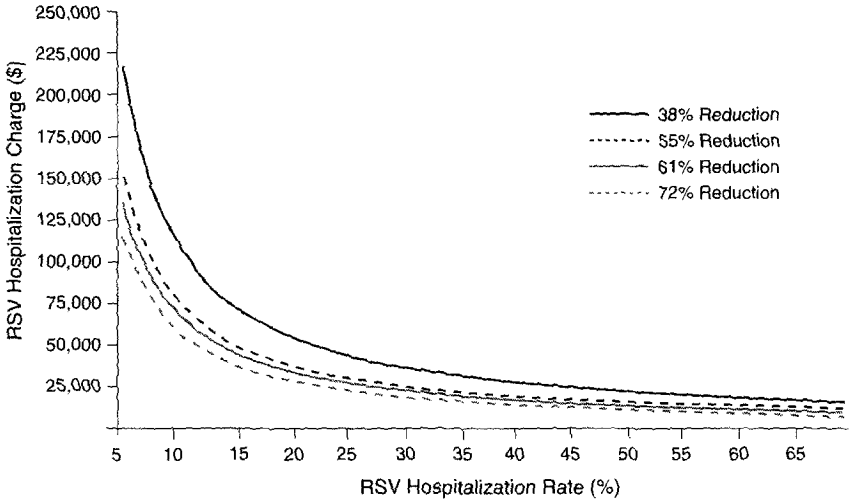

Figure 2. Break-even analysis of all premature infants who did and did not receive palivizumab prophylaxis for respiratory syncytial virus (RSV). Values below boundary lines in graph indicate additional spending for infants receiving prophylaxis; values above boundary lines indicate cost savings with palivizumab prophylaxis.

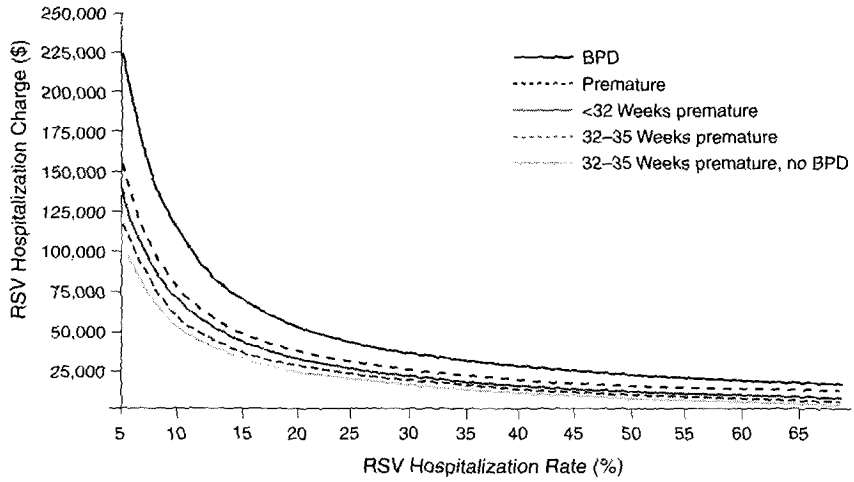

Figure 3. Break-even analysis of high-risk infants who did and did not receive palivizumab prophylaxis for respiratory syncytial virus (RSV). Values below boundary lines in graph indicate additional spending for infants receiving prophylaxis; values above boundary lines indicate cost savings with palivizumab prophylaxis. BPD = bronchopulmonary dysplasia.

DISCUSSION AND CONCLUSIONS

Health economic analyses of RSV infection, management of infected infants, and the passive immunity achieved with palivizumab depend on many factors. Because data on potential long-term sequelae of early RSV infection are scarce, hospitalization rates and initial expenses associated with acute RSV-related lower respiratory infection determine in large part the current burden of illness. Hospitalization rates have been substantially lower in clinical trials than in observational studies, and initial hospital charges constitute only a portion of the total expenses incurred by infected infants. Secondary and possibly even tertiary hospital stays would substantially increase the expense of treating infections and strengthen the rationale for prophylaxis. To date, secondary hospitalization rates have not been determined. For these reasons, observational trials currently provide the best data from which to derive estimates of the economic impact of RSV prophylaxis.

Obviously, costs relating to the prophylaxis and treatment of infections are dependent on the duration of the economic assessment (time horizon of study) and the resources consumed during the full period of care. If neonatal RSV infection is truly linked to the development of reactive airway disease (eg, asthma), then resource consumption by affected individuals would be lifelong, as would the related expense.

Finally, the size (approximately 325,000 infants/season) and demographic characteristics of at-risk populations dramatically influence calculations. If all at-risk infants received prophylaxis, costs and benefits would be maximized; on the other hand, if palivizumab was given only to infants with the greatest risk, the costs of prophylaxis and the overall benefits would be minimized.

Beyond these considerations are the humanistic and ethical concerns that must be addressed before the benefits and limitations of RSV prophylaxis can be fully understood. For example, neonatal quality-of-life concerns are never assessed and rarely discussed. There are ethical and moral issues involved in withholding a treatment (ie, prophylaxis) that has been shown to be well tolerated, efficacious, and cost-effective.[20,31] All these matters deserve consideration, because their resolution will help guide clinical decisions.

This analysis indicates that widespread clinical use of prophylactic palivizumab will have effects ranging from expected incremental charges of ≤$3459 per infant to expected savings of ≤$39,107 per infant.

ACKNOWLEDGMENTS

This research was funded through an unrestricted grant from MedImmune, Inc., Gaithersburg, Maryland, and was conducted independently of that company.

Expert clinicians consulted about the components of care for treating RSV infection included the following: John DeVincenzo, MD, Assistant Professor of Pediatrics in Infectious Diseases, University of Tennessee, Memphis, Tennessee; Hugh E. Evans, MD, Professor of Pediatrics, University of Medicine and Dentistry of New Jersey, Newark, New Jersey; Eric A. Simoes, MD, DCH, Associate Professor, Pediatrics, University of Colorado Health Sciences Center, Denver, Colorado; Elaine B. St. John, MD, Associate Professor of Pediatrics, University of Alabama, Birmingham, Alabama; and Todd Wandstrat, PharmD, Assistant Professor of Clinical Pharmacy, Adjunct Assistant Professor of Pediatrics, Robert C. Byrd Health Sciences Center, West Virginia University, Charleston, West Virginia.

Address correspondence to: Albert Marchetti, MD, Health Economics Research, Physicians World Communications Group, 400 Plaza Drive, Secaucus, NJ 07094.

REFERENCES

1. Culyer AJ. The morality of efficiency in health care—some uncomfortable implications. *Health Econ.* 1992;1:7–18.

2. Gilchrist S, Török TJ, Gary HE Jr, et al. National surveillance for respiratory syncytial virus, United States, 1985–1990. *J Infect Dis.* 1994;170:986–990.

3. Brandenburg AH, Jeannet PY, Steensel-Moll HA, et al. Local variability in respiratory syncytial virus disease severity. *Arch Dis Child.* 1997;77:410–414.

4. Kim PE, Musher DM, Glezen WP, et al. Association of invasive pneumococcal disease with season, atmospheric conditions, air pollution, and the isolation of respiratory viruses. *Clin Infect Dis.* 1996; 22:100–106.

5. Walsh EE, McConnochie KM, Long CE, Hall CB. Severity of respiratory syncytial virus infection is related to virus strain. *J Infect Dis.* 1997;175:814–820.

6. Hall CB, Walsh EE, Schnabel KC, et al. Occurrence of groups A and B of respiratory syncytial virus over 15 years: Associated epidemiologic and clinical characteristics in hospitalized and ambulatory children. *J Infect Dis.* 1990;162:1283–1290.

7. McConnochie KM, Hall CB, Walsh EE, Roghmann KJ. Variation in severity of respiratory syncytial virus infections with subtype. *J Pediatr.* 1990;117:52–62.

8. Lehr MV, Simoes EAF. A weapon against RSV for children at risk. *Contemp Pediatr.* 1998;15:78–90.

9. Wang EEL, Law BJ, Boucher FD, et al. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study of admission and management variation in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. *J Pediatr.* 1996;129:390–395.

10. Schwartz R. Respiratory syncytial virus in infants and children. *Nurse Pract.* 1995; 20:24–29.

11. Dezateux C, Fletcher ME, Dundas I, Stocks J. Infant respiratory function after RSV-proven bronchiolitis. *Am J Respir Crit Care Med.* 1997;155:1349–1355.

12. Sandritter TL, Kraus DM. Respiratory syncytial virus–immunoglobulin intravenous (RSV-IGIV) for respiratory syncytial viral infections, I. *J Pediatr Health Care.* 1997;11:284–291.

13. Holberg CJ, Wright AL, Martinez FD, et al. Risk factors for respiratory syncytial virus-associated lower respiratory illnesses in the first year of life. *Am J Epidemiol.* 1991;133:1135–1151.

14. Emond A, Evans J-A, Howat P. The continuing morbidity and use of health services by preterm infants after discharge from hospital. *Ambul Child Health.* 1997; 3:121–129.

15. Yüksel B, Greenough A. Birth weight and hospital readmission of infants born prematurely. *Arch Pediatr Adolesc Med.* 1994;148:384–388.

16. Yun B-Y, Kim M-R, Park J-Y, et al. Viral etiology and epidemiology of acute lower respiratory tract infections in Korean children. *Pediatr Infect Dis J.* 1995;14: 1054–1059.

17. Wright AL, Taussig LM, Ray CG, et al. The Tucson Children's Respiratory Study. II: Lower respiratory tract illness in the first year of life. *Am J Epidemiol.* 1989; 129:1232–1246.

18. Donati D, Cellesi C, Rossolini A, et al. Serological diagnosis of respiratory viral infections: A five-year study of hospitalised patients. *New Microbiol.* 1998; 21:365–374.

19. Groothuis JR, Simoes EA, Levin MJ, et al. Prophylactic administration of respiratory syncytial virus immune globulin to high-risk infants and young children. *NEJM.* 1993;329:1524–1530.

20. The IMpact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. *Pediatrics.* 1998;102:531–537.

21. The PREVENT Study Group. Reduction of respiratory syncytial virus hospitalization among premature infants and infants with bronchopulmonary dysplasia using respiratory syncytial virus immune globulin prophylaxis. *Pediatrics.* 1997;99:93–99.

22. Oelburg D, Reininger M, Van Eeckout J. A cost-benefit analysis of respiratory syncytial virus hyperimmune globulin (RSV-IVIG) in high-risk infants. *Neonatal Intensive Care.* 1998;January/February:29–33.

23. Abman SH, Ogle JW, Butler-Simon N, et al. Role of respiratory syncytial virus in early hospitalizations for respiratory distress of young infants with cystic fibrosis. *J Pediatr.* 1988;113:826–830.

24. Gurwitz D, Mindorff C, Levison H. Increased incidence of bronchial reactivity in children with a history of bronchiolitis. *J Pediatr.* 1981;98:551–555.

25. Kattan M, Keens TG, Lapierre JG, et al. Pulmonary function abnormalities in symptom-free children after bronchiolitis. *Pediatrics.* 1977;59:683–688.

26. Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. *NEJM.* 1995;332:133–138.

27. Pullan CR, Hey EN. Wheezing, asthma, and pulmonary dysfunction 10 years after infection with respiratory syncytial virus in infancy. *BMJ.* 1982;284:1665–1669.

28. Welliver RC. RSV and chronic asthma. *Lancet.* 1995;346:789–790. Commentary.

29. Buck ML. Prevention and treatment of respiratory syncytial virus—the search for a cost-effective strategy. *Pediatr Pharmacother.* 1997;3:1–3.

30. Cunningham CK, McMillan JA, Gross SJ. Rehospitalization for respiratory illness in infants of less than 32 weeks' gestation. *Pediatrics.* 1991;88:527–532.

31. Hay JW, Ernst RL, Meissner HC. Respiratory syncytial virus immune globulin: A cost effectiveness analysis. *Am J Managed Care.* 1996;2:851–861.

32. Langley JM, Wang EEL, Law BJ, et al. Economic evaluation of respiratory syncytial virus infection in Canadian children: A Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study. *J Pediatr.* 1997;131:113–117.

33. Meissner HC. Economic impact of viral respiratory disease in children. *J Pediatr.* 1994;124(Suppl):S17–S21.

34. O'Shea TM, Sevick MA, Givner LB. Costs and benefits of respiratory syncytial virus immunoglobulin to prevent hospitalization for lower respiratory tract illness in very low birth weight infants. *Pediatr Infect Dis J.* 1998;17:587–593.

35. Robbins JM, Tilford JM, Jacobs RF, et al. A number-needed-to-treat analysis of the use of respiratory syncytial virus immune globulin to prevent hospitalization. *Arch Pediatr Adolesc Med.* 1998;152:358–366.

36. *1998 Drug Topics*® Red Book®. Montvale, NJ: Medical Economics Company; 1998.

37. *Physicians' Current Procedural Terminology: CPT '98.* Chicago: American Medical Association; 1998.

38. Health Care Financing Administration. National Physician Fee Schedule Relative Value File [online public use file]. Updated January 1998. Available at: http://www.hcfa.gov/stats/pufiles.htm. Accessed February 1998.

39. Health Care Financing Administration. Clinical Diagnostic Laboratory Fee Schedule [online public use file]. Updated January 1998. Available at: http://www.hcfa.gov/stats/pufiles.htm. Accessed February 1998.

40. Grier CE, Howe BJ. Economic impact of pneumonia due to respiratory syncytial virus (RSV) infection. Presented at: ICAAC 35th Annual Meeting; 1995; September 17–20, 1995; San Francisco, California.

41. Synagis® (palivizumab) product monograph. Gaithersburg, Md: MedImmune, Inc.; 1998.