INFECTION—Methods and Concepts

USE OF EVIDENCE BASED MODELS TO DEMONSTRATE THE LONG-TERM CLINICAL BENEFITS OF HPV VACCINATION
Bernard L1, Lindsay L2, Rogoza R1, Kohli MA1, Franco EL3
13 Innovus Research Inc, Burlington, ON, Canada. 2GSK Biologicals, Rixensart, Belgium. 3McGill University, Montreal, QC, Canada

OBJECTIVES: Health authorities are keen to understand the clinical benefits and mortality reduction afforded by HPV vaccination for cervical cancer. Complex decision models are not always the most attractive nor the most appropriate means to highlight these benefits. The objective was to develop a relatively simple model to explore the population level impact of an HPV16/18 vaccine.

METHODS: We developed a Monte Carlo model that estimated the absolute number of HPV infections, cervical cancer cases and deaths over the lifetime of a cohort of women. The model estimated the cancer cases and mortality avoided in the presence of vaccination (base-case: 75% vaccine uptake; 95% lifetime efficacy).

RESULTS: Four countries were selected including Germany, Poland, Mexico and Taiwan. Each country has unique patterns of cervical cancer incidence, HPV-type prevalence and cervical cancer screening programs. The model predicted 4584, 4642, 4162 and 37,935 cases of cervical cancer over the lifetime of unvaccinated 10-year-old girls in each of Poland, Germany, Taiwan and Mexico, respectively. Vaccination resulted in a reduction of total cervical cancer cases and deaths of 2392 and 1042 respectively in Poland; 2423 and 857 in Germany; 2143 and 930 in Taiwan and 16,780 and 8381 in Mexico. Sensitivity analyses showed the most critical assumption was the presence of vaccination (base-case: 75% vaccine uptake; 95% lifetime efficacy).

CONCLUSION: Monte Carlo simulation modeling can be a very powerful tool in understanding the potential benefits of vaccination against HPV infection for reducing cervical cancer and specific mortality.

USE OF PHARMACOKINETIC-PHARMACODYNAMIC MODELING WITH MONTE CARLO SIMULATION TO REDUCE ANTIMICROBIAL EXPENDITURES WITHOUT COMPROMISING PREDICTED EFFICACY
Frei CR1, Lewis JS1, Burgess DS1
1University of Texas at Austin and University of Texas Health Science Center at San Antonio, San Antonio, TX, USA. 2University of Texas at Austin and University of Texas Health Science Center at San Antonio and University Health System, San Antonio, TX, USA

OBJECTIVES: Cefepime (CPM) 2g q8h is FDA-approved for the empiric treatment of patients with febrile neutropenia. Pharmacokinetic-pharmacodynamic (PK-PD) studies have demonstrated that cephalosporin efficacy is associated with the percent-time that the free drug concentration exceeds the minimum inhibitory concentration (free %T > MIC). This study compares the free %T > MIC achieved by CPM 2g q8h to four alternative cefepime regimens in an attempt to determine whether antibiotic expenditures can be reduced without compromising predicted efficacy.

METHODS: MIC distributions for Enterobacteriaceae, Pseudomonas aeruginosa, and Acinetobacter baumannii were extracted from the 2002 Intensive Care Unit Surveillance System database. A 10,000-subject Monte Carlo simulation was executed for each species/regimen pair using published PK parameters and these MIC distributions. Cefepime probabilities of target attainment (PTA) were determined for PK-PD targets of ≥50, 60, and 70%T > MIC. PTA for CPM 2g q8h was compared to the PTA of four alternative regimens.

RESULTS: Overall, the 2002 ISS database contained 3543 Enterobacteriaceae (percent susceptible, 95%), 1260 P. aeruginosa (53%), and 271 A. baumannii (15%) isolates. All CPM regimens achieved a PTA similar to that of CPM 2g q8h against Enterobacteriaceae suggesting an opportunity for cost minimization. In addition, CPM 1g q6h achieved equivalent or higher PTA than CPM 2g q8h against P. aeruginosa, and A. baumannii suggesting that the former regimen could be used to achieve similar predicted efficacy at a fraction of the daily cost (4g/d vs. 6g/d). However, the PTA vs. P. aeruginosa and A. baumannii was considerably lower for CPM 1g q8h, 1g q12h, and 2g q12h compared to CPM 2g q8h suggesting that these regimens may not be suitable alternatives for P. aeruginosa or A. baumannii.

CONCLUSION: PK-PD models with Monte Carlo simulation demonstrate that cefepime 2g q8h results in similar predicted efficacy to cefepime 2g q8h despite a reduction in total daily drug of 2g/d.

A REVIEW OF HERD EFFECTS IN THE ECONOMIC EVALUATION OF CHILDHOOD VACCINATIONS
Vicente C1, McKinnon K1, Ciuryla V2, Han D1
1Wyeth Pharmaceuticals, Markham, ON, Canada. 2Wyeth Research, Collegeville, PA, USA

OBJECTIVES: Many childhood vaccines not only protect those directly immunized, but also indirectly prevent infection or disease in the non-immunized population through herd effects. Our objectives were to review the methodological approaches of including indirect benefits of herd effects in economic evaluations of childhood vaccines and to describe the sensitivity of the cost-effectiveness results to herd effects.

METHODS: An extensive systematic review of the literature was conducted. The EMBASE, MEDLINE, Biosis and Current Contents databases were reviewed from 1995–2005. Two independent researchers reviewed titles and abstracts of each article. Additional articles referenced in our primary search were reviewed for further inclusion. Articles meeting inclusion criteria were blinded. Two independent researchers then reviewed and extracted data from all included articles. The quality of each included article was assessed and any discrepancies were resolved through consensus.

RESULTS: Our primary search resulted in 27 titles being identified. Four articles met our inclusion criteria and 23 articles were excluded (7 review papers, 7 non-economic, 7 did not include herd effects and 2 did not assess a childhood vaccine). In each economic evaluation, sensitivity analyses demonstrated that the models were highly sensitive to variations in the estimates of herd effects. In reviewing how herd effects were being captured, various key issues were noted: 1) the source of herd effects and the generalizability from one population to another; 2) the association between herd effects and the vaccine, and 3) implications of a static or dynamic approach to incorporate indirect benefits.

CONCLUSION: The indirect benefits attributed to herd effects have been documented for several vaccines. Economic evaluations have been highly sensitive to variations in herd effects. Improving the precision of measured outcomes attributed to herd effects in future economic evaluations will advance research in this field and assist in health policy decision-making.

MUSCULAR-SKELETAL DISORDERS—Clinical Outcomes Studies

HEALTH TECHNOLOGY ASSESSMENT: EXTRACORPOREAL SHOCK WAVE THERAPY (ESWT) FOR THE TREATMENT OF CHRONIC PLANTAR FASCITIS
Seybold P1, Marangos P1, Papatheofanis F1
1Aequitas, San Diego, CA, USA. 2UCSD, SAN DIEGO, CA, USA

PMS1