Executive Summary for April 2012 SAGE Meeting: Impact on DTP3 Coverage

The impact of new vaccine introduction on the coverage of existing vaccines: a cross-national, multivariable analysis

Jessica C. Shearer[1], Damian G. Walker[2], Nicholas Risko[3], Orin S. Levine[3]
1. Centre for Health Economics and Policy Analysis, McMaster University, Canada
2. The Bill and Melinda Gates Foundation, Seattle, WA, USA
3. International Vaccine Access Center, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Introduction

Few empirical data exist to describe the effect of new vaccine introduction on the immunization system, including its ability to deliver existing, routine vaccines. While limited in their scope and quality, findings from the published and grey literature reviews indicate that NUVI may affect service delivery of other vaccines.

This analysis was conceptualised with a view of providing empirical data to support or refute associations between NUVI and routine immunization service delivery, as measured by immunization coverage of three doses of diptheria-tetanus-pertussis (DTP3). To that end, this study used a quantitative approach to explore this question, building eventually into a set of cross-national multivariable models that compare changes in DTP3 coverage across years and between countries to confirm whether these changes are associated with the introduction of a new vaccine. The full version of these results is available on the SAGE website.

Methods

Choice of dependent variable
DTP3 coverage – a measure of the proportion of surviving one year olds who have received three doses of diphtheria, tetanus, and pertussis vaccine – is often used as a proxy for immunization system performance. DTP3 is available for nearly all countries and years in recent decades. We used the UNICEF/WHO Joint Reports. In the regression models, DTP3 is measured for the year following vaccine introduction amongst children aged 12-23 months who were born in the year that the new vaccine was introduced.

Independent variables
The dataset includes 176 countries 2000-2009 with introductions of Hepatitis B (HepB), *Haemophilous influenzae* type b (Hib) and rotavirus-containing vaccines that occurred during these years. NUVI covariates are binary variables reflecting NUVI introductions for a given country-year. Multiple simultaneous introductions were also coded.

A literature review identified other possible determinants of DTP3 coverage. These included socio-economic status, parental education and knowledge, costs and lost wages, previous utilization of health services, social perceptions, geographic access,

staff availability, and natural disaster and conflict. These were predominantly from individual- and community-level studies; only one includes NUVI as a determinant. At the cross-national level, determinants of national coverage included wealth, belonging to UNICEF or PAHO vaccine funds, democracy, decentralization, health worker density, and GAVI Alliance (GAVI) expenditures. The final list of covariates were chosen to reflect these possible factors.

Descriptive analysis methods

Descriptive analyses explored trends and patterns in DTP3 coverage since 2000. Univariate ordinary-least square and logit regression models were used to identify possible relationships of single covariates to DTP3.

Limitations

These data represent NUVI introductions until 2008 but do not include pneumococcal or HPV introductions due to inadequate data. Rotavirus introductions are limited during this period, particularly within low-income countries and thus must be interpreted with caution. We were constrained in our selection of covariates by those which have existing cross-national data; as such, these models are not able to control for certain predictors of interest. These results cannot establish causality. Finally, while these findings illustrate trends at the aggregate level they miss important aspects of country-specific context.

Results

Descriptive analysis results

Median coverage of DTP3 was substantially lower at baseline for low-income countries compared to other income groups but also increased more dramatically over time in low-income countries. Within income groups, the variance between countries decreased over time such that countries' DTP3 rates are more similar in 2009 than in 2000.

New vaccines were introduced 152 times between 2000 and 2008. Thirty-eight (25%) of these introductions were HepB, eight (5.2%) were DTP-HepB, 11 (7.2%) were Hib, 11 (7.2%) were DTP-Hib, 54 (35.5%) were DTP-HepB-Hib, 17 were rotavirus (11.8%) and 13 (8.5%) were multiple formulations. Prior to 2000, 84 countries (44%) had already introduced at least one new vaccine. Monovalent HepB and Hib introductions were more common in earlier years and introductions of the DTP-HepB-Hib combination were more common later (median introduction years: 2002.5 for HepB; 2003 for Hib; 2005.7 for DTP-HepB-Hib).

We explored whether changes in coverage occurred in the year following NUVI. Both declines and increases in DTP3 were observed in post-NUVI years but were no more common than those observed in non-NUVI years.

Multivariate methods

These models attempt to explain whether NUVI, controlling for other determinants of immunization coverage, were associated with DTP3 coverage in years 2001-2009. Mixed-effect multivariable models with random intercepts and coefficients best fit these data. Non-linearity of DTP3 coverage was addressed with a year^2 term. The final models explain changes in DTP3 coverage within and between countries.

Selection of covariates

Each covariate was individually regressed on DTP3 in mixed effect models with year and year^2. Covariates significant at the $p<0.10$ level in these models were entered into the multivariable mixed effects model in a manual step-wise fashion beginning first with new vaccine introduction. Covariates were retained if their addition produced a significant likelihood ratio test result as compared to the previous model; otherwise, they were dropped. Interaction terms were tested in the final models but none (GAVI-eligibility and new vaccine introduction; gross national income (GNI) per capita and new vaccine introduction; GNI/capita and income group) improved model fit. Graphs of observed versus predicted values in the final model suggest adequate model fit. Statistical analyses were performed using Stata 9.0 (College Station, TX).

Results of the multivariable models

The final mixed effects model includes sixteen covariates for 176 countries which contribute 1312 country-years of observations. Countries dropped from the model due to missing data were typically very small population countries and small island states. Please see the full paper for variable means and coefficients.

Year and year^2 were highly significant, exhibiting a positive but diminishing association with DTP3 coverage over time. The introductions of seven formulations of new vaccines were tested in comparison to no introduction. HepB and pentavalent introductions showed no association with DTP3, controlling for other modelled covariates. The small number of observations for DTP-HepB, Hib, DTP-Hib, multiple, and rotavirus suggest caution in interpreting those results.

While initially significant, GAVI eligibility became non-significant upon the addition of other indicators of national income and development. Overall, DTP3 coverage was associated most strongly with other factors such as the existence of war or civil conflict, coverage of antenatal care, infant mortality, and health expenditure per capita.

GAVI-eligible countries

The final GAVI-only mixed-effects model included 73 countries which contributed 648 country-years of observation, and fourteen covariates. As in the global model, DTP3's positive association with year diminished with each successive year. In the GAVI-only model, adequate data demonstrated that there was no association between the

introduction of HepB or pentavalent vaccines and DTP3 coverage. Instead, DTP3 coverage was associated with conflict, infant mortality, and the proportion of roads that are paved. See the full paper for complete tables of findings.

Additional Comments

The introduction of new and underutilized vaccines during 2000-2008 was not positively or negatively associated with DTP3 coverage in 176 countries modelled. Decision-makers can interpret these findings to mean that the introduction of new vaccines should not, *a priori*, be expected to have a pronounced effect on routine immunization coverage. However, continued, careful efforts related to planning and implementation should be pursued, particularly in light of dozens of introductions planned before 2015, sometimes for multiple formulations. While our statistical modelling exercise provides generalized insights, decision-makers and their partners must carefully consider their local context when planning for a new vaccine introduction.