Effect of the Global Alliance for Vaccines and Immunisation on diphtheria, tetanus, and pertussis vaccine coverage: an independent assessment

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Summary

Background **The Global Alliance for Vaccines and Immunisation (GAVI) was created in 1999 to enable even the poorest countries to provide vaccines to all children. We aimed to assess the effect of GAVI on combined diphtheria, tetanus, and pertussis vaccine (DTP3) coverage.**

Methods **We examined the relation between DTP3 coverage for GAVI recipient countries from 1995 to 2004 and immunisation services support (ISS) and non-ISS expenditure per surviving child, controlling for income per head and local political governance variables. We analysed DTP3 coverage reported by governments and estimated by WHO/UNICEF. We also investigated the effect of GAVI on country reporting behaviour.**

Results **In countries with DTP3 coverage of 65% or less at baseline, ISS spending per surviving child had a significant positive effect on DTP3 coverage (p=0·0005). This effect was not present in countries with DTP3 coverage of 65–80% or 80% or more at baseline. If ISS expenditure only is assessed, the estimated cost per additional child immunised in countries with baseline coverage of 65% or less is US$14 and if ISS and non-ISS expenditures are included the cost per child is almost $20.**

Interpretation **The success of ISS funding in countries with baseline DTP3 coverage of 65% or less provides evidence that a public-private partnership can work to reverse a negative trend in global health and that performance-related disbursement can work in some settings. Because ISS funding seems to have no effect in countries with baseline coverage greater than 65%, GAVI should consider redistributing its resources to countries with the lowest coverage.**

Introduction

The Global Alliance for Vaccines and Immunisation (GAVI) is a public-private global health partnership created in 1999, at a time when immunisation coverage was dropping in many countries, to enable even the poorest countries to provide vaccines to all children.[1,2] Countries with a gross national income of less than US$1000 per head per year are eligible to receive financial support from GAVI. Countries with DTP3 coverage below 80% can apply for 5 years of funding for immunisation services support (ISS) to finance the development of immunisation services as part of the health system; countries with combined diphtheria, tetanus, and pertussis vaccine (DTP3) coverage greater than 50% are eligible for new and under-used vaccines support—ie, vaccines against hepatitis B, *Haemophilus influenzae* type b (Hib), and yellow fever, and associated safe injection equipment. All GAVI-eligible countries can apply for injection safety support for 3 years.

By the end of 2005, GAVI had received pledges from government and private sources that totalled US$3·3 billion and provided financial support to 73 of 75 eligible countries. 53 countries received ISS support, 63 received new and under-used vaccines support, and 69 received injection safety support. Between 2000 and 2005, total GAVI disbursements were $760·5 million, of which $124·5 million (16%) was for ISS. The new International Finance Facility for Immunisation, launched in September, 2005, with pledges of $4 billion over the next 10 years, provides a major new source of funds for GAVI's work.[3]

Assessment of the effect of GAVI is important not only because of the alliance's mission and the resources devoted to this effort but also because the project represents an important innovation in global health. Together with Stop TB and Roll Back Malaria, GAVI was one of the first major global health initiatives designed to create new public-private partnerships to tackle major health problems. GAVI is also unique because it leaves decisions on how resources are spent to achieve agreed yearly immunisation coverage targets to the individual recipients themselves.

Countries that apply for ISS from GAVI propose to increase basic immunisation coverage, as measured by DTP3 coverage, by a particular number of children by the end of 5 years. Grants are awarded for 5 years. Grant budgeting is done on the basis that GAVI will disburse $20 per additional child immunised. The cost per child is estimated to be $17 at current coverage, $20 to reach at least 80% coverage, and $25 to expand to greater than 80% coverage.[4] Disbursement in the first 2 years is done on the basis of the estimated number of extra children to be immunised. After the first 2 years, disbursements are given as rewards for achieving increased immunisation coverage. In principle, reward disbursement in year 3 is given on the basis of the number of additional children immunised in year 2, and disbursement in year 4 is on the

basis of the number of children immunised in year 3, etc. Countries are not required to provide detailed plans on how the funding will be used to expand immunisation coverage.

The original GAVI plan called for implementation of reward funding after the first 2 years. However, rewards are only granted to countries with validated reporting of the number of additional immunised children the previous year. Audits of the quality of immunisation data[5] done in eight countries suggest that in some countries the quality of routine immunisation coverage data is not robust enough to use for such performance-related disbursements.[6] Countries whose information systems prove inadequate in a data quality audit[7] are allowed to use predicted numbers of children for year 3 disbursements but not after year 3. By the end of 2005, 20 countries had received reward payments (eight countries in 2004, 12 in 2005), and 17 deferred payments because of continuing problems with their data systems.

Two critical questions are central to current thinking on global health: has GAVI succeeded in raising immunisation coverage? And has the cost to GAVI per additional child immunised been close to $20 per child? A review of the effect of GAVI showed that, for selected countries, immunisation coverage has increased.[8] However, the review did not attempt to control for other factors that might have explained the increase in coverage—eg, rising income per head. Others have calculated immunisation costs and estimated overall costs of increasing DTP3 coverage to 80% in all countries; their results underscore the large financing gap that persists and greatly exceeds funding raised by GAVI thus far.[9–13]

Unlike other major global health initiatives—eg, the Global Fund to Fight AIDS, Tuberculosis and Malaria—for which there is no reliable indicator of effect on health, an almost complete time series of DTP3 coverage is available to assess the effect of GAVI. Our aim was to do a systematic analysis to examine the effect of GAVI spending on DTP3 coverage.

Methods

Measurement of DT3 coverage

We used two different dependent variables—DTP3 coverage reported by governments[14] and DTP3 coverage estimated by WHO/UNICEF[15]—to study the relation between DTP3 coverage for GAVI recipient countries from 1995 to 2004 and various measures of GAVI expenditure per child. There were a few missing values for both sets of coverage. DTP3 coverage is calculated as the number of children who received their third dose of DTP3 by the age of 12 months divided by the number of children surviving to their first birthday. The correlation coefficient for the two measures was 0·88 for GAVI recipient countries. Mean values of reported and estimated DTP3 coverage were 69·8% and 67·1%, respectively. WHO/UNICEF estimates were constructed on the basis of officially reported data by WHO member states, the historical database maintained by UNICEF, published work (mainly coverage survey results and methods), and unpublished surveys available from ministries of health. In our sample, about 54% of country-year estimates had the same DTP3 coverage indicators in both data sets. We did analyses for both the reported and estimated figures. To test the sensitivity of our findings, we used coverage estimates in log terms as dependent variables; the scale change did not alter qualitative results.

We were concerned with the validity of measuring changes in coverage by time with officially reported data. Murray and colleagues[16] assessed the accuracy of officially reported DTP3 coverage rate with estimates generated from household Demographic and Health Surveys.[16] They showed that officially reported DTP3 coverage is higher than that reported in household surveys. However, even if officially reported data and WHO/UNICEF figures are, on average, overestimations of true DTP3 coverage, the analysis undertaken here will be biased only if countries over-reported their coverage estimates to obtain funds from GAVI.

To investigate the validity of country-reported and WHO/UNICEF-estimated DTP3 coverage for this analysis, we analysed 42 available Demographic and Health Surveys done between 1995 and 2004. Estimates from these surveys are nationally representative and are regarded as a valid source of information about childhood immunisation. We constructed two measures of DTP3 coverage: crude coverage, which refers to the proportion of children surviving to their first birthday who received the third dose of DTP3 according to an immunisation card or their mother's report, and valid coverage, which refers to the proportion of children surviving to their first birthday who received the third dose of DTP3 before their first birthday, as recorded on the immunisation card presented to the interviewer. Children were counted in the year that they had their first birthday. To keep uncertainty to a minimum, estimates used in the analyses come from years for which the number of children reaching age 1 year was greater than 300 children per year per survey. Demographic and Health Surveys record immunisation history for children born in the 3 or 5 years before the survey.

For those country-years that a Demographic and Health Survey was available, we examined whether officially reported DTP3 coverage was related to GAVI spending after controlling for either crude or valid coverage measured in the surveys. We regressed country-reported and WHO/UNICEF-estimated DTP3 coverage as the dependent variables on coverage measured in the surveys (either crude or valid), ISS expenditure per surviving child, or total GAVI spending per surviving child. Eight models were tested and the detailed results are shown in webtable 1 and webtable 2. In all models tested, there was no significant relation between country-reported or WHO/UNICEF-estimated DTP3 coverage and the measure of GAVI spending per surviving child after controlling for true coverage measured in the Demographic and Health

See Online for webtables 1 and 2

See Online for webtables 3, 4, and 5

Surveys. These results provide strong evidence that our subsequent analysis of the effect of GAVI spending on DTP3 coverage will not be biased by over-reporting.

There were 66 countries in our final analysis. On the basis of simple descriptive patterns, we expected the effect of GAVI expenditure to differ in countries with different levels of starting coverage and therefore divided countries into three groups on the basis of baseline DTP3 coverage in 2000: 65% or less (29 countries), 65–80% (13 countries), and greater than 80% (24 countries). Countries that received their first GAVI disbursements after mid-year 2004 (Cuba, Solomon Island, Nicaragua, Timor Leste, Papua New Guinea, Somalia, Bolivia, Mongolia, and Honduras) were excluded from the analysis since there would not have been time to see an effect.

Models

We ran three different sets of models. In the first set, we investigated the effect of total GAVI spending on DTP3 coverage, with total GAVI spending per child as an independent variable (webtable 3). In the second set, we examined the targeted effect of ISS spending on DTP3 coverage, with ISS spending per surviving child as an independent variable (webtable 4). We expected the relation between ISS spending per surviving child and DTP3 coverage to be the most direct. Finally, to test whether there were spillover effects of new and under-used vaccines support or injection safety support on DTP3 coverage, we ran models that included both the ISS spending and non-ISS spending as independent variables. The correlation between these two variables was around 0·40, indicating that the identification of an effect of either when both are present might be hard because of possible colinearity.

We controlled for other determinants of immunisation coverage in the analysis by including GDP per head (in international dollars, base year 2000) and other variables. Health spending per head could not be included in the analysis since these data were not available for 2004. Restricting the analysis to 1995–2003 would substantially reduce the power to identify a GAVI effect. We also included the World Bank governance indicators to explore the extent to which governance, policies, and institutional development make a difference. The World Bank governance indicators capture the political, economic, and institutional dimensions of governance: voice and accountability, political stability, government effectiveness, regulatory quality, rule of law, and control of corruption. These composite indicators, with more than 350 variables drawn for many sources, have been measured for more than 200 countries between 1996 and 2004. Indicators for the six governance domains are measured in units ranging from –2·5 to 2·5, with higher values corresponding to better governance outcomes.[17]

The correlation between these governance measures ranged from 0·42 to 0·77. After running models with all governance indicators included individually, to avoid multicolinearity, we used the variable with consistently the strongest relation with DTP3 coverage—political stability and the absence of violence. This variable combines several indicators that measure perceptions of the likelihood that the government in power will be destabilised or overthrown. This indicator was also seen to be predictive of the effectiveness of international aid[18] and Global Fund disbursements.[19] Webtable 5 shows the descriptive statistics of all independent variables.

We did not include other expenditures on immunisation services, whether from national sources or other donors, in the analysis for two reasons. First, estimates of total immunisation expenditure are not available for many years, and complete national health accounts done with consistent methods and approaches have not been developed.[20,21] Second, the question we seek to ask is not what the marginal effect of GAVI funding is given all other financing sources, but rather what is the total effect of GAVI as a programme, including its effects on

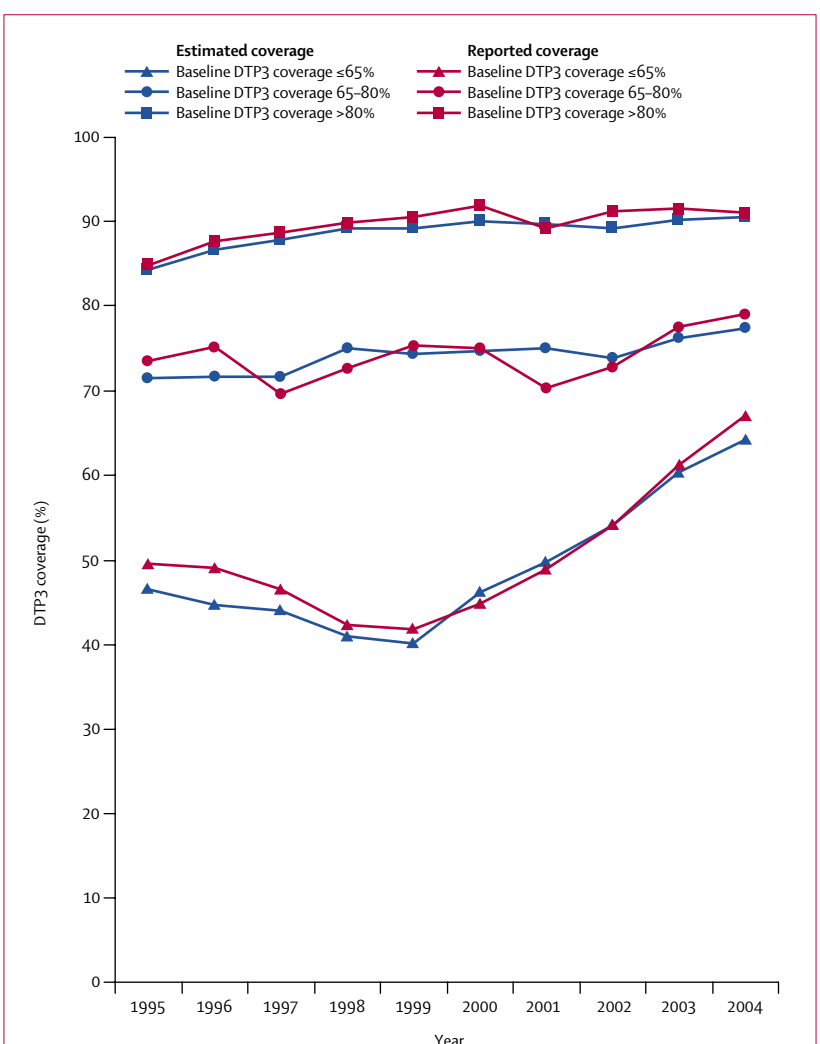

Figure 1: **Mean DTP3 coverage**

increasing or decreasing other sources of finance for immunisation programmes?

Statistical analysis

We used various methods to investigate the effect of GAVI spending on DTP3 coverage with this time-series and cross-sectional data, including the ordinary least squares model with panel corrected SE (PCSE) suggested by Beck and Katz[22–25] and the fixed effects model with Huber-White SE recommended by Kristensen and Wawro.[26] The Wooldridge test for autocorrelation in panel data showed that the hypothesis of zero correlation between error terms within countries is rejected. To deal with serial autocorrelation present in this dataset, we included the 1-year lag of DTP3 coverage in the PCSE model, which also corrects for heteroskedasticity. We also tested for the existence of unit-specific effects and reject the null hypothesis of zero effects. A fixed effects model with Huber-White SE was used to test the sensitivity of our findings from the PCSE model. Since the correlation between fixed effects and independent variables was small for countries with a baseline DTP3 coverage of 65% or less and for countries with a baseline coverage greater than 80%, we present our results from the PCSE model following Kristensen and Wawro suggestions.[26] Details of the various tests, regression results generated from various estimation methods, and model specifications are provided in the webappendix. Regression results for the effect of GAVI spending on improving DTP3 coverage were robust to model specifications. STATA version 9.2 was used for all statistical analyses.

Role of funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all data in the study and C J L Murray had final responsibility for the decision to submit for publication.

Results

Figure 1 shows mean DTP3 coverage from 1995 to 2004. Although the exact time trend differs for the country-reported data and WHO/UNICEF-estimated data, decreases in coverage seen in the 1990s seemed to reverse around 2000 for countries with baseline coverage of 65% or less. Increases in coverage between 2000 and 2004 were most pronounced for countries starting with the lowest level of coverage. The fall in coverage in the 1990s reversed before GAVI disbursement, coinciding with increased policy attention to immunisation during the period that GAVI was created. We did not record a clear upward trend in DTP3 coverage since 2000 for countries with DTP3 coverage greater than 65%.

Trends in mean ISS and non-ISS spending per surviving child are shown in figure 2 and figure 3. ISS spending per child for countries with DTP3 coverage of 65% or less increased steadily over time. This increase

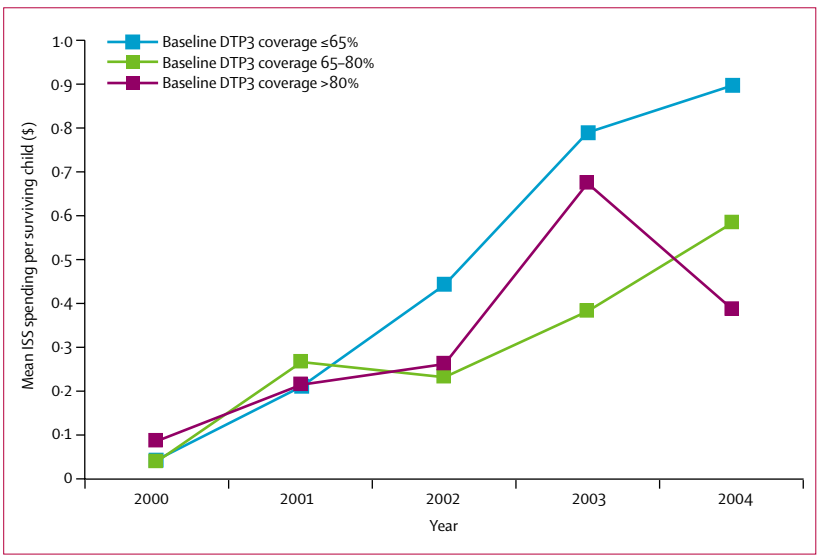

Figure 2: **Mean ISS spending per surviving child**

was largely attributable to the initiation of more project agreements with new countries in subsequent years. For non-ISS spending, expenditure per child in countries with DTP3 coverage greater than 65% at baseline has increased rapidly. With the application criteria, non-ISS spending has been growing at a much slower pace in the lowest coverage group.

See Online for webappendix

Table 1 summarises the analysis of factors influencing DTP3 coverage from the PCSE model. For all three subgroups, the 1-year lag of DTP3 coverage was significant (p=0·0005). The positive sign of 1-year lag DTP3 coverage indicates that DTP3 coverage in the previous year has a positive association with the DTP3 coverage in the current year. The lag variable was not significant for countries with baseline DTP3 coverage of 65–80% in the

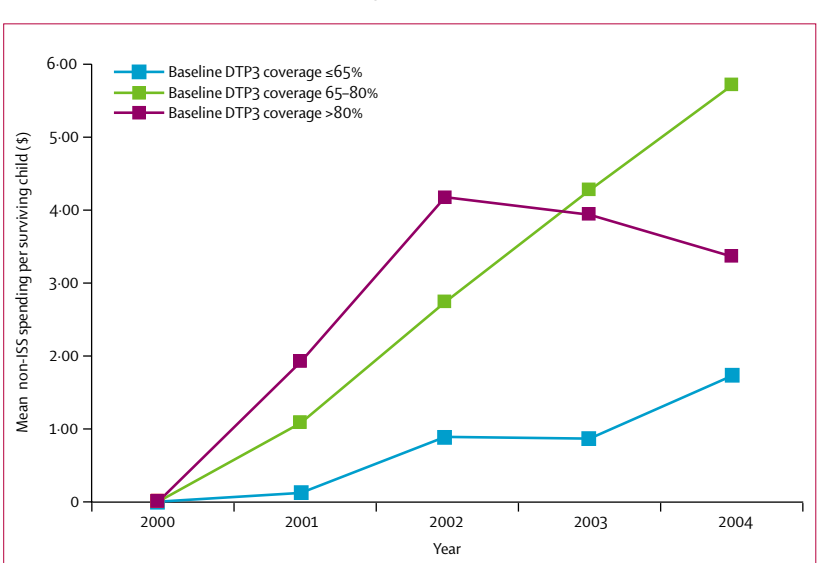

Figure 3: **Mean non-ISS spending per surviving child**

fixed effect model (webtable 4). The results for both reported and estimated coverage were much the same in this respect in the 65–80% coverage group. The effect of income, as measured by the log of annual income per head, was significant for the 65% or under and over 80% coverage groups (p=0·004 and p=0·0005, respectively), but not in the 65–80% group. This result suggests that, holding everything else constant, the greater the income level, the greater the DTP3 coverage will be. This result was sensitive to specifications of the estimation method: with the fixed effects models, including the lag of DTP3 coverage, the effect of income disappeared for these two groups (webtable 4 and webtable 6). Increasing political stability had a positive effect on DTP3 coverage for countries in the group with coverage of 65% or less when both estimated and reported coverage data were used. This finding was robust across various model specifications.

See Online for webtable 6

ISS spending per surviving child had a significant positive effect on DTP3 coverage in countries with baseline DTP3 coverage of 65% or less (p=0·0005). This effect was not present in the other two groups. The coefficients for the effect of ISS spending per head were nearly identical when either reported or estimated data were used. In regressions that included non-ISS spending to test for the effects of injection safety support and support for new and under-used vaccines on DTP3 delivery, the coefficient for ISS spending per surviving child was slightly lower than that from the first set of regressions and still significant in countries with baseline coverage of 65% or less (p=0·009). The positive effect of ISS was present when both the estimated and reported coverage data were analysed with various estimation methods and model specifications. The coefficient on non-ISS spending was positive and significant for countries with baseline DTP3 coverage of 65% or less (p=0·0005), suggesting that funds spent on new vaccines and injection safety indirectly result in increases in DTP3 coverage. However, this finding should be interpreted cautiously, since the effect was not significant when the dependent variables were on a logarithmic scale.

Analysis of the ISS spending coefficient with the lag of DTP3 coverage included in the model allowed us to measure the effect of ISS spending per surviving child on increasing DTP3 coverage over the previous year's level—ie, the coefficient provides an estimate of the marginal cost to GAVI of increasing DTP3 coverage through ISS funding. However, the coefficient does not show the marginal or average cost of immunisation to the country because only GAVI expenditures have been included in the model. By use of the ISS spending coefficient generated by the second set of models that we ran with WHO/UNICEF estimates as the dependent variable as an example, the coefficient implies that increasing ISS spending by $1 per child will increase the coverage by 7·11%. Thus, increasing ISS spending by $100 per child will increase coverage by 711% over the previous level of coverage. The estimated cost to GAVI for each additional child is $14 (ie, $100 divided by 7·11). Table 2 summarises the estimated cost of ISS per

	Baseline DTP3 coverage ≤65%				Baseline DTP3 coverage 65–80%				Baseline DTP3 coverage >80%			
	Estimated		Reported		Estimated		Reported		Estimated		Reported	
	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE	Coefficient	SE
Model 1												
ISS spending per surviving child (US$)	**7·11**	**1·85**	**7·18**	**2·05**	–2·16	2·75	–1·65	–3·31	–0·88	1·64	0·73	1·72
Log (GDP per head)	**5·58**	**1·93**	**5·60**	**2·02**	–1·61	0·89	–1·36	1·63	**3·52**	**0·78**	**2·56**	**0·80**
Political stability index	**3·96**	**0·37**	**2·41**	**0·68**	**2·56**	**0·64**	1·33	1·12	0·51	0·53	–0·18	0·74
Lag of 1 year	**0·35**	**0·07**	**0·36**	**0·08**	**0·18**	**0·04**	**0·18**	**0·06**	**0·11**	**0·03**	**0·12**	**0·04**
Constant	–3·3	12·6	–3·4	12·4	**75·9**	**6·3**	**73·5**	**11·3**	**53·9**	**5·58**	**60·8**	**5·9**
R^2	0·45	..	0·35	..	0·22	..	0·13	..	0·21	..	0·16	
Number of observations	249	..	243	..	124	..	134	..	207	..	207	
Model 2												
ISS spending per surviving child (US$)	**5·01**	**1·92**	**5·29**	**2·31**	–3·11	3·57	–3·39	3·27	–0·45	1·53	1·26	1·74
Non-ISS spending per surviving child (US$)	**1·86**	**0·35**	**1·45**	**0·44**	0·20	0·32	0·63	0·36	–0·21	0·18	–0·23	0·26
Log (GDP per head)	**5·80**	**1·85**	**5·91**	**1·77**	–1·41	0·78	–0·65	1·39	**3·63**	**0·76**	2·68	**0·79**
Political stability index	**4·16**	**0·38**	**2·59**	**0·74**	**2·49**	**0·70**	1·19	1·16	0·53	0·52	–0·13	0·70
Lag of 1 year	**0·33**	**0·07**	**0·33**	**0·07**	**0·17**	**0·04**	**0·17**	**0·05**	**0·11**	**0·03**	0·12	**0·04**
Constant	–4·0	12·4	–4·6	11·1	**74·6**	**5·5**	**68·7**	**9·3**	**53·1**	**5·5**	60·0	**6·0**
R^2	0·47	..	0·37	..	0·22	..	0·14	..	0·21	..	0·17	..
Number of observations	249	..	243	..	124	..	134	..	207	..	207	..

Coefficients significant at the 0·05 level are in bold. PCSE=ordinary least squares with panel corrected SE. Model 1=model to examine the effect of ISS spending on DTP3 coverage. Model 2=model to examine the effect of ISS and non-ISS spending on DTP3 coverage.

Table 1: **Regression results with WHO/UNICEF-estimated or country-reported DTP3 coverage as dependent variables from PCSE models**

surviving child to GAVI for countries with baseline DTP3 coverage of 65% or less generated by our different models for this group of countries. If only ISS expenditure is included in the model, the estimated cost to GAVI per additional child immunised ranges from $8·40 to $14·10. If both ISS and non-ISS are included, the estimated cost to GAVI per additional child immunised ranged from $9·80 to $20. In most of the country-years in this analysis, GAVI disbursement was not done on the basis of the reward system but on $20 per planned additional child immunised. The estimated cost of ISS per child immunised is close to that proposed by GAVI; the 95% CI was wide only when the PCSE model was used. Costs per additional child immunised have not been computed for countries with baseline coverage greater than 65% because we did not identify a significant effect in these groups.

For countries with baseline DTP3 coverage greater than 65%, GAVI spending had no positive effect on coverage. This result was consistent across all estimation methods and model specifications. With the fixed effects model, we noted that ISS spending was negatively associated with the DTP3 coverage for countries with baseline coverage of 65–80%. However, this finding was significant only when WHO/UNICEF estimates were used as dependent variables and should not be given serious weight because of its dependence on model specifications.

Although there has been considerable discussion about the difference between reported and estimated DTP3 coverage for specific countries, in this aggregate analysis, we noted almost no substantive difference in the results for the reported and estimated figures.

To investigate whether GAVI selects countries with the lowest baseline levels of DTP3 coverage on the basis of attributes that might favour success in raising DTP3 coverage, we looked at the number of countries receiving ISS spending in this group. If there were a significant number of GAVI-eligible countries with low DTP3 coverage that did not receive GAVI funding, the possibility of selection bias would be of concern. However, we saw that there was no selection bias in countries with baseline DTP3 coverage of 65% or lower, since all countries in this group (except India) obtained ISS funding from GAVI.

The timing of the effect of GAVI disbursements is also an important issue. We assumed that country behaviour is determined not by the exact timing of the arrival of funds but by the expectation of receiving funds in a particular budget cycle. Webtables 7 and 8 present results from an alternative assumption of the timing of effects (ie, that ISS spending requires a 1-year lag to have an effect). The results are consistent across the two assumptions (ie, when assuming either the expectation of obtaining GAVI funds affects DTP3 coverage or assuming the effect will be seen 1 year later).

	PCSE	FE_RSE (1)	FE_RSE (2)
WHO/UNICEF coverage			
Model 1	14·1 (9·3–29·2)	8·5 (6·6–12·0)	9·7 (7·4–14·3)
Model 2	20·0 (11·4–80·5)	9·6 (7·1–14·6)	11·0 (8·0–17·6)
Country-reported coverage			
Model 1	13·9 (8·9–31·7)	8·4 (6·3–12·6)	9·2 (6·7–14·6)
Model 2	18·9 (10·1–156·3)	9·8 (6·9–16·7)	9·0 (6·5–14·4)

Data are estimated cost in US$ (95% CI). FE_RSE=fixed effects model with robust SE. PCSE=ordinary least squares with panel corrected SE. Model 1=model to examine the effect of ISS spending on DTP3 coverage. Model 2=model to examine the effect of ISS and non-ISS spending on DTP3 coverage.

Table 2: **Estimated ISS cost per additional immunised child for countries with baseline coverage of 65% or less**

Discussion

This independent assessment of the effect of GAVI on DTP3 coverage shows that GAVI has contributed to increased DTP3 coverage in countries with baseline DTP3 coverage of 65% or less at their first approval for GAVI funding. We estimate the cost to GAVI to be about $8·40–20 per additional child immunised. This estimate is close to the proposed cost to GAVI of $20 per additional immunised child. Since most of the disbursements analysed here were initial funding payments rather than reward payments, our results provide evidence that the original estimation of additional cost per fully immunised child for these countries was a reasonable approximation. Furthermore, the success of ISS funding for countries with baseline coverage of 65% or less provides evidence that a public-private partnership can help to reverse a negative trend in global health. Although many of the payments that countries received during the period analysed were made on the basis of planned increases in child immunisation, we believe that our results can be interpreted as a success for performance-related disbursement. The behaviour of countries with respect to GAVI funds was most likely affected by the prospect that reward payments would begin in the third or fourth year of the projects. Performance-related disbursements should be carefully analysed in the coming years so that behaviour of a greater number of countries than at present can be observed during the reward phase of GAVI funding.

The absence of an effect of ISS funding on DTP3 coverage in countries with baseline coverage greater than 65% is concerning, especially since about 40% of total ISS funds from 2000 to 2004 have been spent in such countries. Why do these resources have no demonstrable effect? Did these resources help to prevent recorded levels of coverage from dropping? We propose four possible explanations.

See Online for webtables 7 and 8

First, GAVI resources might have increased DTP3 coverage, but the effect could have been too small to identify in this rigorous analytical framework. However, we successfully identified an effect in countries with low starting coverage. The fact that the model does not show an effect of GAVI spending for countries in the two

groups with the highest coverage could be related to a ceiling effect—ie, achieving increases in the time studied is more difficult for countries that have high levels of coverage to begin with. However, we saw no effect when we increased the power to identify potential ceiling effects (webtable 9 and webtable 10).

See Online for webtables 9 and 10

Second, GAVI resources in these countries could have simply crowded out more generous national budgets for health and thus have had no effect on total immunisation spending. If true, this explanation could indicate that the effect of performance-related disbursement is associated with the relative—not the absolute—magnitude of the reward. If country political and managerial attention for immunisation programmes is driven by the size of rewards relative to national health budgets, performance-related disbursement in middle income or better off countries could be unaffordable. The WHO immunisation financing database, which is meant to track other financial flows for immunisation, could provide data to explore this possibility.

Third, the cost of increasing DTP3 coverage in these countries could be so high that GAVI resources were not sufficient to bring about an effect. If this were the case, would such costs be a high priority for global health? Again, the WHO immunisation financing database could provide data to explore this possibility.

Finally, GAVI resources could have helped to maintain DTP3 coverage. Maintainence of coverage levels, however, is not GAVI's mission. ISS is the financial support provided to national governments for the development of immunisation services, aiming to stimulate increases in routine immunisation coverage. This analysis cannot provide empirical evidence that GAVI resources helped to maintain coverage, in part because robust measures of national expenditures on immunisation are not available.

Although further analysis is clearly warranted, if the goal of ISS spending remains to increase DTP3 coverage, spending resources in countries with baseline coverage greater than 65% with the present ISS approach might not have benefits. By contrast, GAVI resources are having a positive effect on DTP3 coverage in countries with coverage of 65% or less; if there is scope for absorbing increased ISS resources in these countries, GAVI should consider increasing investments in ISS funding for them.

If a $20 per additional child immunised performance-related disbursement does not work in countries once coverage levels of 65% have been achieved, what will work to raise immunisation coverage? This analysis provides no insight into what policy options might be considered. We urgently need to explore whether the problem in these countries is related to the size of the reward, competing health priorities, or health system bottlenecks such as physical and financial access to health services for disadvantaged populations.

We have not examined the effect of GAVI on expanding coverage of new vaccines. Clearly, the target of resources for new and under-used vaccines support is to increase coverage of immunisations for hepatitis B and Hib and to accelerate the introduction of pentavalent vaccines, especially in countries with weak health systems. The increased cost of adopting new vaccine formulations is much larger than had been expected and thus poses particular challenges for the long-term sustainability of immunisation programmes.[27] Coverage information for these vaccines is not complete and several more years of experience might be needed before a similar time-series cross-sectional analysis of the effect of new and under-used vaccines support can be done.

Is the effect of GAVI in the low baseline coverage countries sustainable? There has been considerable debate about sustainability, and the original philosophy of GAVI was to leverage its resources so that, in the long run, national expenditures will replace GAVI expenditures.[12,28] It is far too early to assess this type of effect. In the medium term, the effect of GAVI is sustainable only if very low-income countries are able to find the increased resources from national and external sources. The demonstration that, in these countries, GAVI resources have an effect at an affordable cost is important, since it could help sustain international finance for a longer period in the poorest countries.

We have not examined the effect of GAVI investments on the rest of the health system. Several workers[29–33] have expressed concerns that GAVI investments, like other international externally financed initiatives, could distort national priorities and lead to reductions in the delivery of other health services. Others have argued that GAVI might build health systems.[34] The potential negative side-effects of GAVI funding on national priorities and the delivery of other health services has been at the core of GAVI board deliberations,[35] which concluded that supporting national priorities and strengthening national health systems is a high priority but should not distract GAVI from its main goal—to increase immunisation coverage and support wider access to new and underused vaccines. We have identified no reasonable way of testing either of these hypotheses with the available data. The externalities of GAVI and other global health initiatives are an extremely important topic and one that should be researched carefully. Data necessary to assess these effects should be more systematically gathered in the future.

The current and future success of GAVI is fundamentally linked to the capacity to measure the output of immunisation programmes through changes in immunisation coverage. In this analysis, we have shown that both reported and estimated DTP3 coverage are not biased by GAVI payments. We have also shown that GAVI resources have much the same effect when both country-reported data and WHO/UNICEF-estimated data are used. Nevertheless, there remains a possibility that, in the future, as GAVI payments increase, reported and estimated DTP3 coverage could be affected by GAVI disbursements. Household survey data and the

WHO/UNICEF-estimated figures provide substantially different results, and change over time can be quite different. GAVI's own work on data quality audits has also highlighted the deficiencies of routine service delivery monitoring in many countries. A high priority for GAVI should be to develop a multifaceted approach to immunisation coverage, routine measurement, and periodic validation in all countries.

Contributors

C Lu and C J L Murray participated in model design, statistical analysis, and writing of the report; C M Michaud participated in data collection, literature review, and writing of the report; E Gakidou participated in the statistical analysis of Demographic and Health Surveys and their relation to GAVI spending; K Khan participated in data collection and statistical analysis.

Conflict of interest statement

We declare that we have no conflict of interest.

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