OHE Consulting

A division of the Office of Health Economics

Summary report
December 2006

DONOR INVESTMENT CHOICES FOR GLOBAL HEALTH:
Modelling the value for money of investing in Product Development, Public Private Partnerships as compared to other health care interventions

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SUMMARY

Objective To model the cost-effectiveness for donors of investing in R&D projects into global diseases via public private partnerships for product development (PD PPPs).

Methods We modelled the R&D process for drug and vaccine development projects in HIV/AIDS, malaria and TB using a Markov model. We estimated rates of uptake of a new technology in individual countries across three WHO regions based on its cost-effectiveness relative to a GDP/capita willingness to pay threshold, the cost-effectiveness of existing interventions and an assumed budget. An efficiency criterion was imposed on the use of current technologies.

Results For vaccine PD PPPs the portfolio cost per DALY averted ranged from $12 to $107 depending upon budget assumptions whilst, for drugs, it ranged from $12 to $17. Compared with published cost-effectiveness ratios for existing programmes and with plausible cost-effectiveness benchmarks for developing countries, these results look very promising.

Conclusions The study provides a framework for assessing, and preliminary indications of, the cost-effectiveness of PD PPPs. Donors may wish to compare these results with the returns from alternative uses of funds.

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1. INTRODUCTION

1.1 Context and emerging economic issues

Potential donors have limited resources to invest in new product development through public private partnerships for product development (PD PPPs). In many cases these donors are already funding existing treatments and have the option to invest more in these treatments rather than in R&D for new treatments. They have a strong interest to identify where the next dollar or equivalent would obtain the greatest return. There are several economic evaluation programmes underway to assess the yield from investing more in existing technologies, with the WHO-CHOICE and Disease Control Priorities Project (DCPP) initiatives amongst others. Not surprisingly, stakeholders in the field are commenting that it is the right time to begin an evaluation process in relation to PD PPPs.

1.2 Aims of study

In this study, we set out to assess the cost-effectiveness of the PD PPP R&D process, from the perspective of a donor that is only financing R&D costs and not the costs of distribution and therapy on the market. The return to the donor is the social health benefit derived from the discovery and use of new treatments in target regions (SEAR-D, AFRICA D and AFRICA E[1]). The focus is on PD PPPs developing drugs or vaccines for HIV-AIDS, tuberculosis or malaria, namely:

- Global Alliance for TB Drug Development (TB Alliance),
- Medicines for Malaria Venture (MMV),

[1]We used epidemiological regions as applied in WHO-CHOICE studies. See http://www.who.int/choice/demography/en/

Submitted by: OHE Consulting, 12 Whitehall, London SW1A 2DY UK

Kindly funded by The Rockefeller Foundation and overseen by a Steering Group: David Evans (WHO), Charles Gardner (Rockefeller Foundation), Rob Hecht (IAVI), Dean Jamison (UCSF), Hannah Kettler (Bill and Melinda Gates Foundation), Catherine Porter (DFID).

OHE Consulting remains solely responsible for any errors in the analysis. Elements of the study will be submitted to peer review journals.

- International Partnership for Microbicides (IPM),
- International AIDS Vaccine Initiative (IAVI),
- Malaria Vaccine Initiative (MVI),
- Aeras Global TB Vaccine Foundation (Aeras).

Our analysis only considers the direct benefits generated by the development of new products. We acknowledge that the innovative activities conducted by PD PPPs create additional R&D spillovers (e.g. contributing to the scientific knowledge advancement in the field) and encompass a broader range of important initiatives, including advocacy to increase the global commitment to innovation for diseases of poverty through the involvement of local communities and the financial support of national governments and philanthropic foundations.

A secondary objective of the study is to identify the key drivers of cost-effectiveness, such that stakeholders can identify new questions and areas for more focused investigation as PD PPPs evolve.

2. METHODS

We developed a method for estimating the costs (from the perspective of donors) of investing in the R&D process and the likely health benefits that might accrue to developing countries as a result, in order to estimate the R&D cost per DALY[2] averted for the donor. This involved:

- modelling the R&D process;
- estimating the DALYs averted from the outputs of the R&D process.

2.1 Modelling R&D yield

We modelled the R&D process using a Markov multi-state model, similar to the life cycle financial model of pharmaceutical R&D developed by Myers and Howe (1997)[3]. In our version of this model, a representative portfolio of investigated entities is assumed to start at the discovery stage. Subsequent stages of the model follow the usual cycle from Phase I through Phase III and then to registration and market approval.

At the point where a vaccine or drug from the representative portfolio receives marketing approval, the model assigns a reward which captures the expected return in terms of DALYs averted from the adoption of that product. The ratio of the present value of R&D costs and the present value of DALYs averted gives us the estimated R&D cost per DALY averted for the representative R&D programme.

[2]DALY is a Disability Adjusted Life Year which measures the loss of life and disability caused by disease.

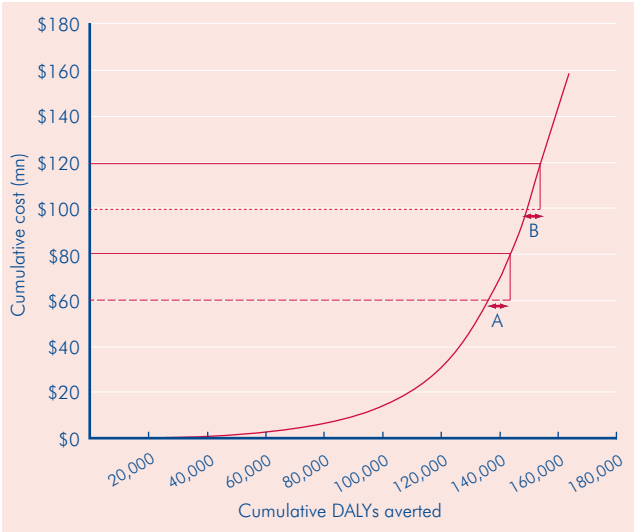
[3]Myers S, Howe C. (1997). "A Life-Cycle Financial Model of Pharmaceutical R&D". Working Paper 41-97. Cambridge MA, Program on the Pharmaceutical Industry, Sloan School of Management, MIT. Ref Type: Serial (Book, Monograph).

2.2 Uptake of new technologies

We assessed the benefits of R&D to develop a new drug or vaccine in terms of its impact on the health of those within developing countries who are vaccinated or are treated with the new drug. This impact is expressed in terms of DALYs averted.

We have assumed that introducing a new vaccine or drug in a developing country involves a corresponding reduction in spending on other types of health care. To illustrate how our model deals with this, we use the concept of the cost-effectiveness frontier, a hypothetical example of which is presented as the curved line in Figure 1.

Figure 1: Cost-effectiveness frontier



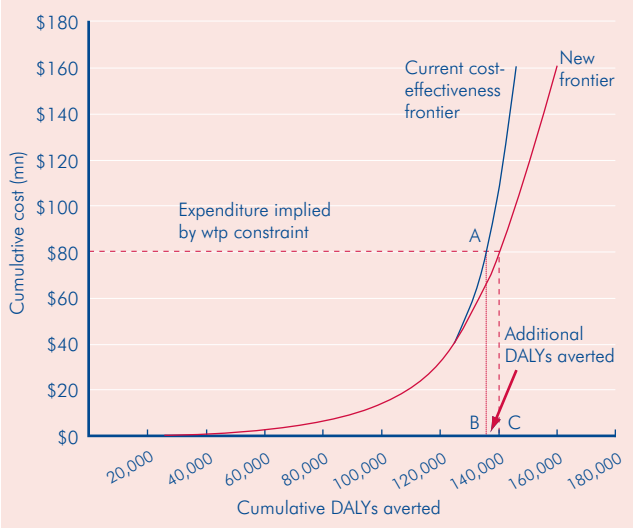
The frontier shows, for a given level of expenditure in a particular disease area, the greatest improvement in health (DALYs averted) which is possible with currently available treatments. Points to the right of the line cannot be reached with current treatments while, to the left of the frontier, health care expenditure is not being used to its best effect because an increase in DALYs averted could be achieved at any given level of spending. We assume that each country's spending has the greatest possible impact on DALYs, thus placing it on the frontier. However, the frontier shows only what is possible with a given level of spending; it does not tell us how much is being spent.

In the absence of information on actual levels of spending in specific disease areas within a country, we may consider that, as the level of expenditure increases, the impact on DALYs of further spending decreases. Compare, for example, the DALYs averted by an increase in spending from $60 mn to $80 mn (the dashed line A) with the DALYs averted from an increase in spending from $100 to $120 mn (the dotted line B). At some point on the frontier, the DALYs averted from an increase in spending will be deemed too small to justify the additional spending.

This limit occurs when the extra spending required to avert one extra DALY (the cost per DALY averted) exceeds a country's willingness to pay (wtp) to avert DALYs. In the base case, we assume this to be equal to a country's GDP per capita, reflecting the overall resources available. The use of GDP per capita as a basis to model developing countries wtp is a widely accepted practice. It was proposed by WHO in 2002 and is still recommended by the WHO-CHOICE initiative[4].

Let us suppose that this limit is reached in our hypothetical example at an expenditure of $80 mn (Figure 2). With the set of treatments available at any point in time, a country can reduce the disease burden only by increasing expenditure. However, the introduction of a new drug or vaccine opens up new opportunities for a country. Provided that the new drug or vaccine has a greater impact on the DALY burden than at least one of the treatments currently used, i.e. has a lower cost per DALY averted, it will be worthwhile adopting in place of those existing treatments with a relatively high cost per DALY averted. The impact on DALYs is illustrated in Figure 1 by the 'New frontier' line. Within the current level of spending, the increase in DALYs is equal to the distance BC.

Figure 2: Introduction of new technology



The limitation of this approach (referred to as the ringfenced option) is that it assumes no possibility of moving expenditure between different disease areas. Therefore, we examined the impact of two other budget scenarios which allow the reallocation of health funds across disease areas. In one, we assumed that the proportion of total health care expenditure accounted for by each disease area is equal to that disease's share of the total DALY burden of disease (DALY share). In the other scenario, we assumed that the entire health care budget was potentially available to the new technology (the unrestricted approach). In the event that the DALY share and unrestricted approaches result in additional expenditure over and above the notional level derived from the frontier, we made an assumption about the DALY benefits lost from those treatments which would thus be displaced.

[4]WHO (2002). World Health Report 2002. Geneva: World Health Organization. See also http://www.who.int/choice/costs/CER_thresholds/en/index.html

3. RESULTS

3.1 Base case results

Table 1 presents our final base case results aggregated into two notional portfolios, one for vaccines and the other for drugs. They share all our base case assumptions, including our local demand assumptions based on the following budget scenarios (see also Section 2.2):

- ringfenced, where funds are limited by current spending in each disease area and new interventions are adopted if they are more cost-effective than existing interventions;
- DALY share, where funds are limited by the proportion of national health budget equal to DALY share of disease in each country;
- unrestricted, where new interventions are fully adopted if cost-effective (i.e. cost per DALY below GDP per capita)

The cost per successful portfolio is obtained assuming that investments in each of the specific product areas have been modelled until a successful product emerges and is approved for market. Costs and DALY benefits associated with these products are aggregated into a vaccine total and a drugs total.

Table 1 Base case results for notional portfolios

	Cost per successful portfolio ($mill)	Cumulative DALYs averted per successful portfolio (mill)	R&D costs per DALY averted
Vaccines			
Ringfenced	4951.36	46.22	107.13
DALY share	4951.36	138.75	35.69
Unrestricted	4951.36	407.42	12.15
Drugs			
Ringfenced	1593.46	109.73	14.52
DALY share	1593.46	94.21	16.91
Unrestricted	1593.46	127.97	12.45

3.2 Sensitivity analysis results

We explore how our results are sensitive to a number of assumptions, including the demand for new products, attrition rates for product development, discount rates and time horizon. Alternative estimates of demand for new products can have an impact on results. However, the cost-effectiveness ratios remain favourable even under the alternative scenarios we considered, and the sensitivity analyses do not alter the basic conclusions of the study.

3.3 Key takeaways

For vaccine PD PPPs the portfolio cost per DALY averted ranged from $12 to $107 depending upon budget assumptions. The vaccine portfolio was therefore more sensitive to varying the budget assumption than the drugs portfolio, for which the range of cost per DALY averted was $12 to $17. Behind these aggregate figures lie variations in our cost-effectiveness estimates according to the individual R&D projects we have modelled.

Compared with published cost-effectiveness ratios for existing programmes and with plausible cost-effectiveness benchmarks for developing countries, such as $100 per DALY proposed by the World Bank[5] and GDP per capita in these regions used by WHO-CHOICE[6], these results look very promising.

4. DISCUSSION

4.1 Assumptions and limitations

The most challenging aspect of the study has been generating data to populate the model. In particular, estimating the R&D yield is highly problematic. There are issues to do with R&D costs per phase, but the main areas of uncertainty are probabilities of success and estimates of the effectiveness of new products.

We do not take account of any R&D spillovers. Many PD PPPs see their role as stimulating R&D by others as well as that they directly fund themselves. Furthermore, our analysis does not incorporate potential benefits from long-term solutions to problems such as drug resistance, which is particularly important for malaria. All these elements may considerably enhance the cost-effectiveness of PD PPPs investment options.

This analysis was undertaken by comparing existing treatments and new treatments in a world where purchasers funded the most cost-effective medicines. We know that this is not the case in practice, but in the long term (the model has a 40 year time horizon), countries may move closer to achieving this. However, from the perspective of health versus non-health resource allocation decisions, it might distort the picture in favour of health.

Our analysis considers only three WHO regions which cover most of the disease burden for HIV and malaria but only around half for TB. The inclusion of other regions of the world where TB has a high burden (e.g. Eastern Europe) could increase significantly the health gains generated by new products in this area, especially by a new TB vaccine.

Another limiting factor is that we could not consider the interactions between PD PPPs. Vaccine and drug programmes evaluated were not seen as competing with each other for the scarce budget resources of the recipient countries. This could have a major impact in some cases, e.g. where take-up of a PD PPP drug/vaccine would be significantly curtailed because another more cost-effective PD PPP drug/vaccine had been developed for the same disease.

4.2 Donor considerations

As was indicated above, donors need to consider the long term outcomes from a system-wide perspective, which includes addressing the issue of drug resistance. That being said, the political significance of saving lives now, with a fair degree of certainty, versus saving lives later, with a high degree of uncertainty, cannot be overlooked.

One of the most important issues for donors to consider is whether they will have to pay for uptake of new products in the future, as well as funding the R&D itself. This clearly has financial implications and might alter the cost-effectiveness ratios for donors. We have not addressed this issue in our study, but it would be a valuable question to research at some future point.

5. CONCLUSIONS

The portfolio cost per DALY averted for vaccine PD PPPs ranged from $12 to $107 depending upon budget assumptions. For drugs, the portfolio range was $12 to $17. Compared with published cost-effectiveness ratios for existing programmes and in relation to cost-effectiveness benchmarks for developing countries, such as $100 per DALY and average GDP per capita in these regions, these results look very promising.

From an investment perspective it would be best to adopt a portfolio approach, as donors can reduce risk by funding a portfolio of R&D ventures whose drivers of success/failure are largely unrelated.

Empirical information on PD PPP R&D productivity is still limited. We would recommend that a further evaluation is undertaken in 2-3 years time to assess the validity of our estimates and re-estimate them with additional information on the PD PPPs, and updated estimates of DALY burden and income levels.

[5]See Berndt E, Glennerster R, Kremer M, Lee J, Levine R, Weizsacker G (2005). "Advanced markets for a malaria vaccine: estimating costs and effectiveness"

[6]See WHO-CHOICE website: http://www.who.int/choice/costs/CER_thresholds/en/index.html