CENTRE FOR SUSTAINABILITY AND SOCIAL INNOVATION

Health Economics of Neglected Diseases

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Contents

Executive Summary

The aim of this project was to develop a financial model for valuing economic loss caused by neglected diseases prevalent in developing countries. Treatments are available for these diseases but failure of existing mechanisms of health-care finance and delivery (due to poor management including outdated public health programs that are not focussed on the prevailing conditions, use of incorrect medical interventions and corruption) prevent interventions reaching sufferers[1]. The model consists of three data sets: economic productivity of the healthy population, economic productivity of disease sufferers and the costs of medical intervention. This data was used to create a net present value (NPV) for each intervention.

Using lymphatic filariasis in India as a case study, a model was developed using relevant data from the above data sets. The 15 year NPV of productivity of the healthy population was $43086 USD (3% discount rate) while the comparable NPV of an LF sufferer was $42863 USD – a difference of $223USD. The maximum annual cost of medication was 15 USD (but could be as little as 89 cents) over 15 years. The positive NPV return for chemotherapy was therefore $208 USD using the highest cost medication and $222 USD with the lowest cost option. For patients with advanced disease (hydrocele) surgical intervention is an option. The cost of surgery in India varied between 5.7 USD and 57.1 USD[2].

These findings present a strong economic case for provision of preventative chemotherapy for populations living in endemic areas. Surgical intervention may also provide a positive NPV return if the number of interventions required is minimal and the surgery can be costed at the lower end of the price range. The analysis indicates that the development of health insurance mechanisms for affected communities as an efficient method for financing preventative chemotherapy programs is economically viable. This may provide the basis for investigation of the viability of alternative financing models (e.g. for-profit or non-profit micro-health insurance schemes). A further aim in undertaking this type of analysis is that the development of a financial model will add to the availability of information to policy makers likely improving the decision making process. Finally it is hoped this type of analysis will be a useful tool in the attempt to improve health outcomes amongst the world's poorest people.

[1] Sachs, J.D. (2001) Macroeconomics and Health: Investing in Health for Economic Development. Report of the Commission on Macroeconomics and Health presented to WHO 20 December 2001 http://whqlibdoc.who.int/publications/2001/924154550x.pdf

[2] Ramaiah , K.; Guyatt, H.; Ramu, K.; Vanamail, P.; Pani, S.; Das, P. (1999) Treatment costs and loss of work time to individuals with chronic lymphatic filariasis in rural communities in south India. Tropical Medicine and International Health, 4, 1 pp 19–25

1. What are neglected diseases?

Numerous initiatives by governments, NGOs and philanthropic foundations have targeted the control and treatment of a number of infectious diseases affecting the developing world particularly focusing on HIV/AIDS, tuberculosis and malaria[3]. However this focus on the so-called "big three"[4] has driven down the priority for addressing the challenge posed by a large number of other (infectious) diseases for which there are cost-effective and successful interventions available; these have been called the neglected diseases[5] (ND). NDs include a number of conditions caused mainly by helminths, protozoans, bacteria and viruses. They are variously classified and defined, with narrower definitions including about 13 conditions[6] while a more comprehensive definition is provided by the Public Library of Science Neglected Tropical Diseases, a journal dedicated to the field, which lists 37 conditions[7]. These diseases affect over one billion people[8] and are responsible for over 500,000 deaths per annum as well as causing disability and disfigurement[9].

2. Addressing the neglected diseases

Since 2000, there has been increased global focus on reducing ill-health caused by disease in developing countries. This was largely driven by the establishment of the Millennium Development Goals (MDG) an initiative resulting from the world leaders' summit in 2000[10] and the increased activity of philanthropic foundations such as the Gates Foundation[11]. To this end the Commission for Macroeconomics and Health (CMH) was established by the WHO to "assess the effect of health on economic development" [12]. The CMH found that one effective strategy to drastically improve health in developing countries was to direct existing treatments towards a

[3] Bulletin of the World Health Organization Volume 83, Number 3, March 2005, 161-240
[4] Bulletin of the World Health Organization Volume 83, Number 3, March 2005, 161-240
[5] David H Molyneux (2004) "Neglected" diseases but unrecognised successes— challenges and opportunities for infectious disease control Lancet; 364: 380–83
[6] Hotez, P.J., Molyneux, D.H., Fenwick, A., Kumaresan, J., Ehrlich Sachs, S., Jeffrey D. Sachs, J.D., and Savioli, L. (2007) Control of Neglected Tropical Diseases. New England Journal of Medicine 2007; 357: 1018-27.
[7] PLoS Neglected Tropical Diseases Journal. http://www.plosntds.org/static/scope.action
[8] David O'Connell (2007) Neglected Diseases Nature 449, 7159, 157
[9] Hotez PJ, Ottesen E, Fenwick A, Molyneux D. The neglected tropical diseases: the ancient afflictions of stigma and poverty and the prospects for their control and elimination. Adv Exp Biol Med 2006; 582:22-33.
[10] http://www.un.org/millenniumgoals/bkgd.shtml
[11] http://www.gatesfoundation.org/Pages/home.aspx
[12] Sachs, J.D. (2001) Macroeconomics and Health: Investing in Health for Economic Development. Report of the Commission on Macroeconomics and Health presented to WHO 20 December 2001 http://whqlibdoc.who.int/publications/2001/924154550x.pdf

small number of NDs prevalent in low- or middle-income countries. A CMH follow up report[13] highlighted the importance of not only increasing resources but emphasized the importance of acquiring the knowledge of how best to use the increased health care funding and resources promised in the MDG.

3. The role of the Open Health Initiative

The Open Health Initiative is funded by the Mindset Social Innovation Foundation[14] with a focus to address the issue of NDs. Since existing (mainly) public health care systems in developing countries have failed to reduce the prevalence of NDs[15], the examination of alternative models of drug development and delivery and the investigation of funding mechanisms will be beneficial for determining the viability of alternative financing models. As outlined in the CMH report[16], the investigation and development of finance models will be an invaluable tool in making health care investment decisions. Precedence for the development of alternative models has already been set by a number of initiatives including the Grameen Health Care Trust[17].

3.1 The aim and scope of this project

The internship project relates specifically to development of a costing model to assess the economic viability of providing treatments for NDs. The development of this model is based on the selection and characterization of a disease and its effect on a population living in a given endemic area. The aim of the project is to examine whether it is viable to offer microinsurance to address the issue of NDs.

4. What is microinsurance?

Historically health insurance was conceived as an instrument for mutual protection of the working class during the nineteenth century[18]. Microinsurance is an offshoot of microfinance – the supply of basic financial services to the poor[19]. Microinsurance is a mechanism for providing

[13] Spinaci S., Currat L., Shetty P., Crowell V., Kehler J. (2006) Tough choices: investing in health for development: Experiences from national follow-up to the Commission on Macroeconomics and Health. WHO Publications http://www.who.int/macrohealth/documents/report_and_cover.pdf

[14] http://www.mindsetfoundation.com/

[15] Sachs, J.D. (2001) Macroeconomics and Health: Investing in Health for Economic Development. Report of the Commission on Macroeconomics and Health presented to WHO 20 December 2001 http://whqlibdoc.who.int/publications/2001/924154550x.pdf

[16] Spinaci S., Currat L., Shetty P., Crowell V., Kehler J. (2006) Tough choices: investing in health for development: Experiences from national follow-up to the Commission on Macroeconomics and Health. WHO Publications http://www.who.int/macrohealth/documents/report_and_cover.pdf

[17] http://www.grameenhealth.org/

[18] http://www.ilo.org/wow/Featuredbook/lang--en/WCMS_081384/index.htm

[19] http://www.kiva.org/about/microfinance/

social protection to excluded populations while at the same time creating a new market for the insurance industry[20]. According to the WHO microinsurance requires large volumes of very small policies to be profitable. The administration costs for maintaining each of these policies is high relative to the premiums paid therefore for this type of scheme to become sustainable these costs need to be significantly reduced.

However, attempts thus far aimed at the establishment of sustainable microinsurance schemes have proved elusive. A sustainable business model is seen as a trade-off between three factors:

1. coverage of large numbers of low income populations
2. reduction of administration costs
3. affordability for the target population.

"Successful microinsurance schemes therefore usually involve their members in choosing the benefits and levels of coverage that they can afford."[21]

Two organizations have been pioneers in this area: Grameen Kalyan and Allianz Microinsurance. Grameen Kalyan was established in 1996 as an offshoot of the Grameen Bank in Bangladesh. The business model for Grameen Kalyan is one where the organization provides both insurance and primary health care services. There are 38 health centres in operation and these are usually co-located with a Grameen Bank branch. Grameen Kalyan has a number of sources of income including endowments from Grameen Bank as well as grants from the ILO, but it is also able to generate funds from its microinsurance scheme. This schemes charges $1.73 USD to Grameen Bank members (and $2.17 USD to non-members) in return for insurance of six family members. This includes a free annual check up, while for each additional visit to a health center a cardholder pays an additional $0.14 USD. The insurance scheme is able to offer medicines at discounted prices to members; however, the services provided only cover small risks with a maximum coverage of $29 USD per annum. Rather than providing coverage for major and costly medical interventions, the scheme instead focuses on prophylaxis and education particularly related to maternal health and family planning. Grameen Kalyan treated 321000 patients in 2007 and provided home services to an additional 2.5 million villagers. However, despite the limited coverage and the focus on preventative medicine its operational cost recovery rate has only increased from 38% to 93% between 1997 and 2007 suggesting that the existing microinsurance model is not sustainable without the additional grants and endowments that Grameen Kalyan has received. Grameen Kalyan has started collaborating with Pfizer, GE Healthcare and the Mayo Clinic to find scalable and sustainable health care insurance and delivery models. The results of the collaboration were due to be published in September 2009[22]

[20] http://www.apeseg.org.pe/images/images/4_Churchill_CGAGwg_Presentation.ppt
[21] http://www.ilo.org/wow/Featuredbook/lang--en/WCMS_081384/index.htm
[22] http://www.microcapital.org/microcapital-story-grameen-kalyan-offers-health-microinsurance-for-usd-173-per-year-and-partners-with-pfizer-inc-ge-healthcare-and-mayo-clinic-is-it-economically-viable/

Another example of microinsurance is that of Allianz. Allianz views microinsurance as a market based product characterized by low premiums (affordability), high volumes of business and efficient distribution. Allianz has been one of the pioneers in this new market and its approach has been to partner with NGOs (Care International, Planet Finance) and technical assistance organizations (GTZ, UNDP) to carry out market research and provide training for the establishment of (micro-)insurance professionals in these new markets. Allianz view this business as not only catering for a social need but also providing a longer-term financial return[23]. The Allianz approach is firstly to educate the population (with the assistance of NGO partners) about the concept of insurance while the NGOs also assist in delivery of microinsurance schemes. Allianz has been able to start microinsurance schemes in a number of countries using this strategy including Egypt, Senegal, Indonesia, Colombia and India, the latter offering the most comprehensive range of services including life, accident, property and a community-based health insurance program with a combined total of 242000 policy holders[24]. However there is no indication that this is a profitable model either, rather it is the stated aim of Allianz to learn about these new insurance markets and to build brand awareness amongst policy holders some of whom Allianz anticipates will progress and become future clients of other (presumably more profitable) products[25].

5. Choice of disease and country

Lymphatic filariasis (LF) was selected as the model disease. LF is endemic in 83 countries[26] with about 30% of cases occurring in India. It is, after malaria, the second most common vector borne disease[27]. According to WHO estimates[28] about 120 million people are infected with the disease with a further 1 billion[29] at risk living in endemic areas. Further, LF is the second most important cause of disability worldwide. [30] India was selected as the study country because the highest incidence of LF occurs in India; moreover since the Indian economy is growing rapidly[31] any economic loss due to disease or disability is further magnified.

[23] http://www.allianz.com/en/about_allianz/sustainability/social_impacts/microinsurance/index.html
[24] http://www.allianz.com/en/about_allianz/sustainability/social_impacts/microinsurance/index.html
[25] http://knowledge.allianz.com/en/globalissues/microfinance/microinsurance/microinsurance_egypt_agf.html
[26] http://www.stanford.edu/class/humbio103/ParaSites2006/Lymphatic_filariasis/Epidemiology.htm
[27] Wynd, S.; Carron, J.; Selve, B.; Leggat, P.; Wayne Melrose, W.; Durrheim, D. (2007) Qualitative analysis of the impact of a lymphatic filariasis elimination programme using mass drug administration on Misima Island, Papua New Guinea *Filaria Journal*, 6:1
[28] World Health Organization: *Building partnerships for lymphatic filariasis– strategic plan* Geneva: World Health Organization; 1999.
[29] de Almeida, A.; Freedman, D. (1999) Epidemiology and immunopathology of bancroftian filariasis. Microbes and Infection, 1, 1015−1022; Hotez, P.J., Molyneux, D.H., Fenwick, A., Kumaresan, J., Ehrlich Sachs, S., Jeffrey D. Sachs, J.D., and Savioli, L. (2007) Control of Neglected Tropical Diseases. New England Journal of Medicine 2007; 357: 1018-27.
[30] WHO, 1995 World Health Organization, 1995. World Health Report, Geneva.
[31] https://www.cia.gov/library/publications/the-world-factbook/geos/in.html

5.1 Lymphatic filariasis – pathogen lifecycle, aetiology and distribution

LF is a parasitic disease caused by three species of nematodes (multi-cellular worms)[32] namely - *Wuchereria bancrofti* (WB), *Brugia malayi*, and *Brugia timori*[33]. WB is responsible for 90% of infections whilst the remaining 10% of infections are caused by the two Brugia species.[34,35] WB is the prevalent causative agent of the disease in India[36], the country selected for investigation so the description of the life cycle, infection, diagnosis and treatment will focus on Bancroftian filariasis as this type of LF is also called[37].

The life cycle of WB passes through four stages (Figs. 1 and 2): Infection is caused by female mosquito bites (*Culex quinquefasciatus*, *Anopheles gambiae*, *Anopheles funestus*, and *Aedes polynesiensis* are the most common species of mosquitoes that transmit *Wuchereria bancrofti*.[38,39]) when the third stage infective larvae (L3) parasite is transmitted to the human host during the blood meal of the mosquito through the wound caused by the mosquito bite. After entry to the human host the L3 larvae migrate to the lymphatic system. Between 9 and 14 days after entering the lymphatic system the L3 larvae transform into the fourth stage larvae. The fourth stage L4 larvae then incubate for between 6-12 months in the lymphatic system until maturity when the adult males and females mate. Females then release thousands of sheathed stage one larvae (L1) called microfilariae (*singular*: microfilaria) into the lymphatic system. Microfilariae then enter the blood from the lymphatic system. Microfilariae concentrate in the micro-vessels of the lungs but during the peak time for mosquito bites (10 pm to 2 am – nocturnal periodicity) the microfilariae migrate to peripheral blood. A mosquito biting the infected subject will then ingest some of the microfilariae during its blood meal which are transferred to the mosquito stomach where the microfilariae (L1) lose their sheaths, eventually migrating through the stomach wall (to escape digestion) and boring into the thoracic flight muscles. After approximately 10 days maturation the L1 microfilariae transform to the L2 stage. The L2 stage lasts about two days during which time the larvae moult and develop into the

[32] http://nematode.unl.edu/wormgen.htm
[33] http://www.stanford.edu/class/humbio103/ParaSites2006/Lymphatic_filariasis/Introduction.htm
[34] Molyneux, D.; Bradley, M.; Hoerauf, A.; Dominique Kyelem, D.; Taylor, M. (2003) Mass drug treatment for lymphatic filariasis and onchocerciasis. TRENDS in Parasitology 19, 11, 515-522
[35] Palumbo, E. (2008) Filariasis: diagnosis, treatment and prevention Acta Biomedica; 79: 106-109
[36] Agrawal,V.; Sashindran, V. (2006) Lymphatic Filariasis in India : Problems, Challenges and New Initiatives *MJAFI, Vol. 62, No. 4,359-362*
[37] http://www.stanford.edu/class/humbio103/ParaSites2006/Lymphatic_filariasis/Introduction.htm
[38] Life Cycle of *Wuchereria bancrofti* http://www.filariasis.org/pdfs/lfcycle.pdf.
[39] Different species of the following genera of mosquitoes are vectors of *W. bancrofti* filariasis depending on geographical distribution. Among them are: *Culex* (*C. annulirostris*, *C. bitaeniorhynchus*, *C. quinquefasciatus*, and *C. pipiens*); *Anopheles* (*A. arabinensis*, *A. bancroftii*, *A. farauti*, *A. funestus*, *A. gambiae*, *A. koliensis*, *A. melas*, *A. merus*, *A. punctulatus* and *A. wellcomei*); *Aedes* (*A. aegypti*, *A. aquasalis*, *A. bellator*, *A. cooki*, *A. darlingi*, *A. kochi*, *A. polynesiensis*, *A. pseudoscutellaris*, *A. rotumae*, *A. scapularis*, and *A. vigilax*); *Mansonia* (*M. pseudotitillans*, *M. uniformis*); *Coquillettidia* (*C. juxtamansonia*). (http://www.dpd.cdc.gov/DPDx/HTML/Frames/A-F/Filariasis/body_Filariasis_w_bancrofti.htm)

infective L3 larvae. The L3 larvae migrate from the thorax to the mosquito mouth parts whereupon the next mosquito blood meal of a human results in transmission of the L3 larvae from the mosquito through the bite wound thereby completing the life cycle. An informative animation of the disease life-cycle can be found here.[40]

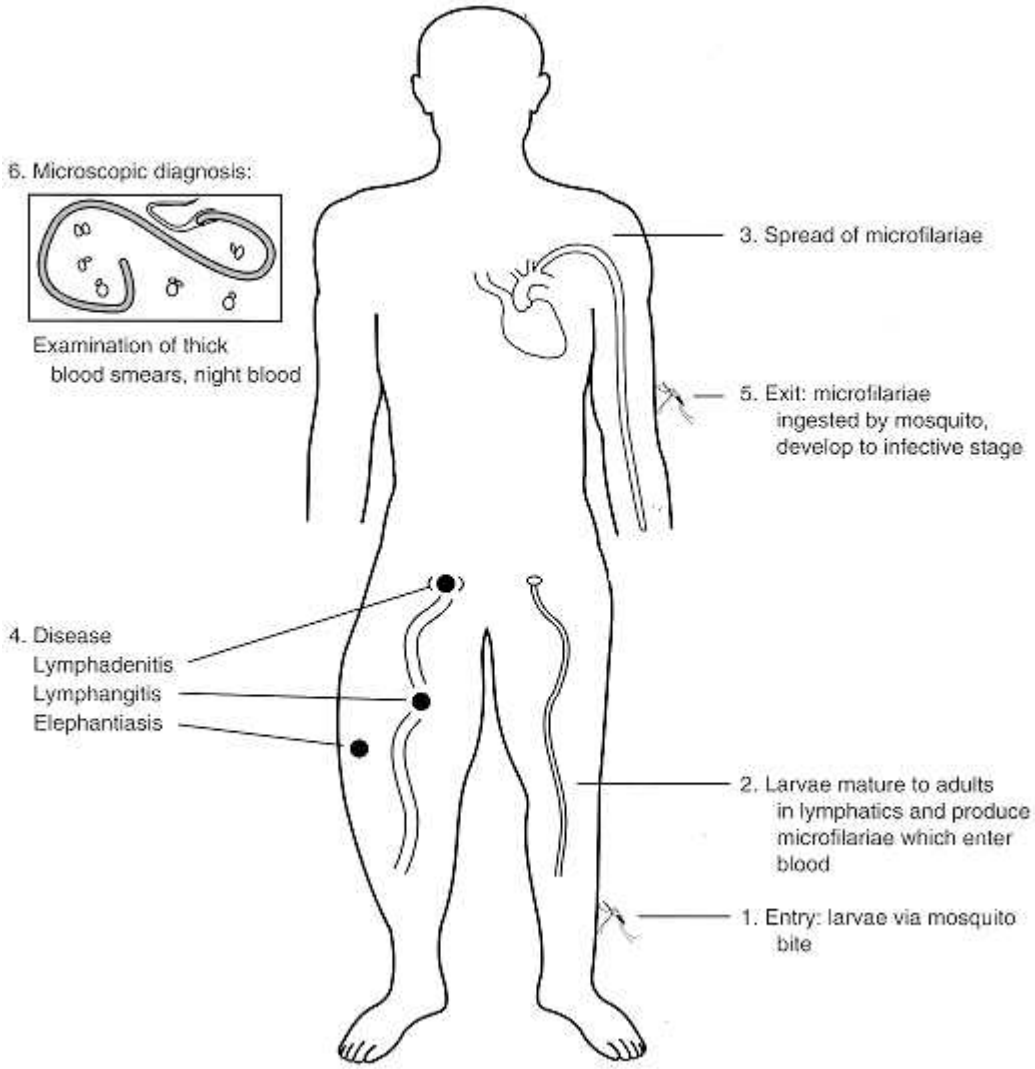

Figure 1 Lifecycle of Wuchereria and Brugia
(Medical Microbiology *Fourth Edition)* http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=mmed&part=A4949

[40] http://www.liquidjigsaw.com/animation/anim1.htm

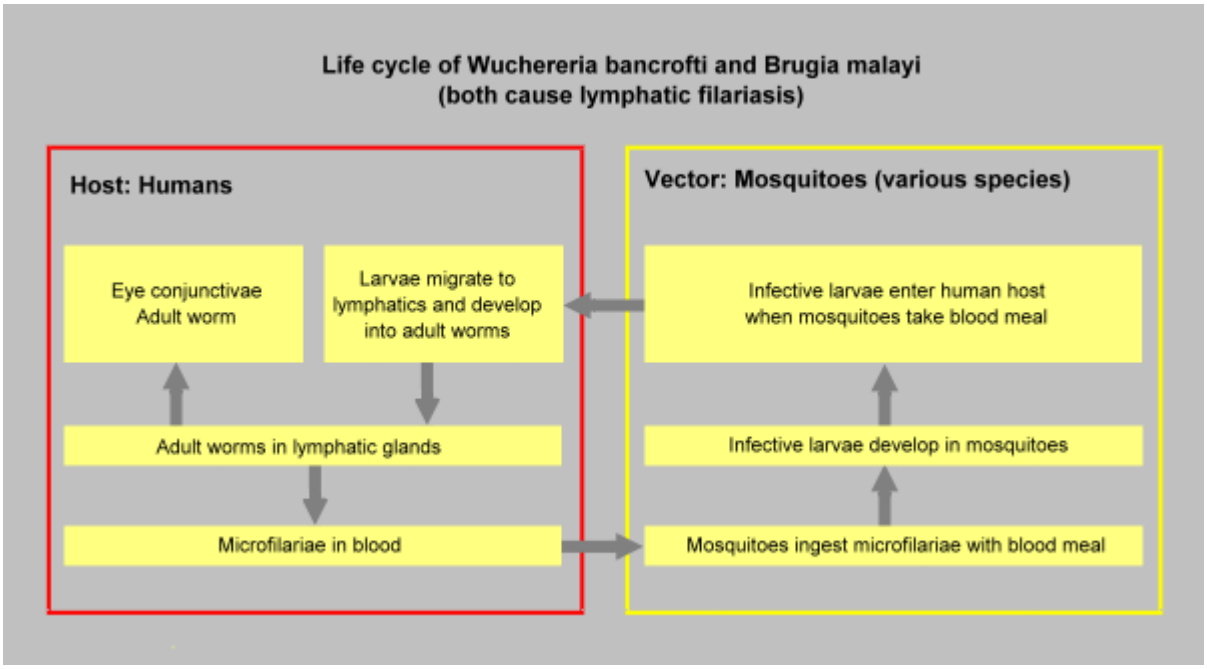

Figure 2 Diagram obtained from http://www.parasite-diagnosis.ch/web/11113/lymphfilaessentials.

From the patient perspective, after infection the disease may be asymptomatic for some time even when microfilariae are found in the blood (the pre-patent period – the time from infection to first detection of microfilariae is one year or more[41], but some abnormalities caused by the disease even at this early stage such as dilation of lymphatic vessels appear to be irreversible even after treatment. The disease then progresses to the acute stages where symptoms manifested include adenolymphangitis (ADL) and acute filarial lymphangitis (AFL)[42]. ADL specifically refers to inflammation of the lymph glands[43,44] and is the most common symptom of the acute phase of the disease. Patients suffer fever, lymphadenopathy (swelling of lymph glands and nodes) in the inguinal canal (groin) and axillae (armpits)[45], accompanied with pain in the affected areas. AFL is caused by dying adult worms and is characterized by the formation of small nodules at the site of worm death resulting in tender and enlarged lymphatics[46] (in men the swelling of the scrotum is known as hydrocele[47]). As the disease advances, the acute swelling associated with the lymphatic system results in permanent gross enlargement of the limbs or genitals (known as lymphoedema or elephantiasis[48]). This morbidity, if untreated is mostly considered lifelong and patients not only suffer from impaired employment opportunities but

[41] http://www.parasite-diagnosis.ch/web/11113/lymphfilaessentials
[42] Paluimbo, E. (2008) Filariasis: diagnosis, treatment and prevention Acta Biomedica 2008; 79: 106-109
[43] http://www.patient.co.uk/doctor/Lymphatic-Filariasis.htm
[44] Babu, B.; Nayak, A. (2003) Treatment costs and work time loss due to episodic adenolymphangitis in lymphatic filariasis patients in rural communities of Orissa, India Tropical Medicine and International Health 8, 12, 1102–1109
[45] http://www.patient.co.uk/doctor/Lymphatic-Filariasis.htm
[46] http://www.patient.co.uk/doctor/Lymphatic-Filariasis.htm
[47] http://www.mayoclinic.com/health/hydrocele/DS00617
[48] http://www.healthlinkbc.ca/kbase/nord/nord689.htm

also from societal discrimination, reduced marriage prospects and reduced sexual (reproductive) life[49].

Limited studies have been performed on the prevalence of LF; however, Michael *et al*.[50] published a meta-analysis of the global prevalence and distribution of LF. Two of the key findings relevant to this study are: the global age distribution of Bancroftian filariasis (Table 1) shows that approximately 15.6% of sufferers are in the 0-15 age group; while the gender profile of Bancroftian filariasis (Table 2) shows that for every female case there are 1.19 male cases (total number of cases column) – this figure comprises the sum of acute infections and chronic stage disease – consisting of 1.36 male infections per female infection and 0.65 male lymphoedema cases per female case. Michael *et al*. further estimate the number of lymphoedema cases in India at approximately 7.4 million (Table 2), while another report[51] estimates that globally, 44 million of 120 million LF sufferers have hydrocele and lymphoedema which equates to approx 11 million sufferers in India (based on 30% of global disease occurring in India).

LF has been described as a disease of poverty which perpetuates poverty – economic loss includes loss of human resources in prevalent areas as well as a loss of productivity (and taxes) to the state.[52] In India (as in many other countries), filariasis is mainly a disease of the poor, prevalent in both urban and rural areas[53].

Age group	Population[a]	Infections[b]	Lymphoedema	Hydrocele	Total no. cases[c]	Prevalence (%)	% of total global cases
0-4	552	2.71	0.13	0.06	2.88	0.52	2.72
5-14	918	11.44	0.94	1.82	13.63	1.48	12.84
15-44	1932	42.76	6.45	15.62	60.72	3.14	57.18
45-59	432	10.7	2.57	5.65	18.13	4.2	17.07
60+	285	5.74	2.44	3.64	10.83	3.8	10.2
Total	4119	73.27	13.21	26.79	106.19	2.58[d]	100

Table 1 Global estimate of the number of cases and prevalence of filariasis (infection and chronic disease) due to WB by age group (from Michael *et al*). a – Population in endemic regions only. b – Microfilaraemia cases only. c – Denotes infection and disease cases

[49] http://www.dcp2.org/pubs/DCP/22/Section/3023

[50] Michael E, Bundy DA, Grenfell BT. (1996) Re-assessing the global prevalence and distribution of lymphatic filariasis. Parasitology. Apr;112:409-28

[51] Haddix, A.; Kestler, A. (2000) Lymphatic filariasis: economic aspects of the disease and programmes for its elimination *Transactions of the Royal Society of Tropical Medicine and Hygiene, 94:* 592-593

[52] Haddix, A.; Kestler, A. (2000) Lymphatic filariasis: economic aspects of the disease and programmes for its elimination *Transactions of the Royal Society of Tropical Medicine and Hygiene, 94:* 592-593

[53] K.D. Ramaiah, P.K. Das, E. Michael and H. Guyatt (2000) The Economic Burden of Lymphatic Filariasis in India *Parasitology Today, 16, 6, 251-253*

Pathogen	Population		Infections[a]		Lymphoedema		Total no. cases[b]	
	M	F	M	F	M	F	M	F
WB	440	410	17	12.46	2.6	3.98	19.6[c]	16.10
BM	440	410	1.11	0.69	0.58	0.28	1.63	0.95

Table 2 Estimates of the number of cases (in millions) of filariasis infection and lymphoedema due to WB by gender in India (adapted from Michael et al.). a – Microfilaraemia cases. b – Infection and chronic disease cases including hydrocele in males. c – the total number of cases for males (i.e. the sum of infections and lymphoedema) is stated as 29.43 in the paper however this is likely to be a typing error and has been corrected to 19.6 here. (M – Male; F – Female).

6. Model Development

Three data series were used as inputs into the model: economic productivity, DALYs – a measure of disease burden and the price of medicines.

6.1 Economic model development:

There are a number of approaches to measuring the economic activity of the working population. This can be measured using earnings[54]; however there is poor availability of wage data for developing countries, (*e.g.* Ramaiah et al[55] obtained wage data by surveying the economic effects of LF through primary research; but this is not an option for development of a generic model). Moreover there is considerable difficulty in making the data comparable because of differences in the way data is measured and there is the requirement for converting to a common unit of currency[56]. Economists therefore tend to measure output either in terms of total productivity or in terms of labour productivity and considerable effort has gone into making this data comparable[57]. This measure of output was used for this study although even availability of this data is not complete since productivity is usually measured in terms of output per hour but for developing countries only the less informative measure of output per worker is available[58]. The

[54] Chiswick, B.R. (2003) Jacob Mincer, Experience and the Distribution of Earnings. IZA Discussion Paper No. 847

[55] Ramaiah, K.D. Ramu, K; Guyatt, H.; Kumar, K.; Pani, S.; (1998) Direct and indirect costs of the acute form of lymphatic filariasis to households in rural areas of Tamil Nadu, south India. *Trop. Med. Int. Health* 3, 108–115

[56] Amiti M. and Stiroh K. (2007) Is the United States Losing Its Productivity Advantage? Current Issues in Economics and Finance 13, 8, September 2007 http://www.newyorkfed.org/research/current_issues/ci13-8.pdf

[57] Specifically the ILO has produced a Key Indicators of the Labour Market program: KILM 5th Edition available freely at http://www.ilo.org/public/english/employment/strat/kilm/

[58] Amiti M. and Stiroh K. (2007) Is the United States Losing Its Productivity Advantage? Current Issues in Economics and Finance 13, 8, September 2007 http://www.newyorkfed.org/research/current_issues/ci13-8.pdf

level of output per worker can then be further characterised into an age distribution since it has been shown that productivity[59] (and wages[60]) vary with age.

In the case study with LF in India, GDP data was obtained from the International Monetary Fund (IMF)[61]. The IMF estimates GDP data up to five years ahead (in this instance until 2014). This is a relatively short forecast period for the purpose of studying disability which may be lifelong therefore a longer term forecast was required. Long-term GDP forecasts are provided by a number of firms on a commercial basis (e.g. Economist Intelligence Unit, EIU[62]). The EIU uses a supply side methodology to make estimates in contrast to short term forecasts which are obtained using a "demand-side framework". Since this data was not freely available long term GDP growth was forecast by using linear regression. A historic year on year growth was calculated and this was also used for forecasting. Data obtained from linear regression was used in the model as this provided the more conservative forecast (See Appendix II Table 14 for details). Estimates for the economically active population were obtained from the KILM database[63] (See Appendix II Table 15, Figs 6 and 7). In order to quantify the economic loss caused by disease, the base level of economic activity for the healthy population was established by calculating forecast productivity per worker (See Appendix I for description of estimation procedures for this data).

6.2 Modelling the effect of disease

It is common practice to evaluate the value of health care programs and interventions in terms of the utility of the health outcomes[64]. Economists have developed, amongst others, two metrics to characterise ill-health: *disability adjusted life years* (DALY) and *quality adjusted life years* (QALY)[65].

The DALY was created by the World Bank in conjunction with WHO and Harvard School of Public Health as a measure of the Global Burden of Disease.[66,67] The DALY measures

[59] Werding, M. (2008) Ageing and Productivity Growth: Are There Macro-level Cohort Effects of Human Capital? CESifo *Working Paper No. 2207*

[60] Mincer (1974) cited in Chiswick, B.R. (2003) Jacob Mincer, Experience and the Distribution of Earnings IZA Discussion Paper No. 847

[61] See Appendix III

[62] http://secure.alacra.com/cgi-bin/alacraswitchISAPI.dll?sk=guest17&app=eiusite&msg=ExecContent&topic=Help&page=ltgintro

[63] http://www.ilo.org/public/english/employment/strat/kilm/

[64] Pinto Prades, José Luis, Abellán Perpiñán, José María María, Mendez, Ildefonso and Badia, Xabier,A Test of the Predictive Validity of Non-linear QALY Models Using Time Trade-off Utilities (February 2004). UPF Economics and Business Working Paper No. 741. Available at SSRN: http://ssrn.com/abstract=563327

[65] Robberstad, B. (2005) QALYs vs DALYs vs LYs gained: What are the differences, and what difference do they make for health care priority setting? Norsk Epidemiologi 2005; 15 (2): 183-191

[66] King, C. and Bertino, A. (2008) Asymmetries of Poverty: Why Global Burden of Disease Valuations Underestimate the Burden of Neglected Tropical Diseases. PLoS Neglected Tropical Diseases Mar 26, 2, 3: e209

[67] Trude Arnesen, T.; Erik Nord, E. (1999) The value of DALY life: problems with ethics and validity of disability adjusted life years *British Medical Journal*;319;1423-1425

population health by combining the years of life lost (YLL) to a disease with the years of life lived in less than perfect health (years lived with disability, YLD)[68]. YLL is a measure of the number of lives lost to a disease multiplied by a function which reflects the premature age of death relative to life expectancies at various ages (as found in standard life tables – for females this is taken as 82.5 years at birth and for males this is taken as 80 years at birth). YLD is estimated by multiplying the number of incident cases of a disease by the average duration in years of the disease until remission or death multiplied by a disability weight that reflects the severity of the illness on a scale of 0 (perfect health) to 1 (death). A panel of experts defines the disability weight[69].

The DALY incorporates two further elements: age weighting and discounting. Age weighting weights a year of life lived at younger or older ages as lower than a year of life lived at ages in between[70]. Although the concept was introduced using evidence from studies which showed that there was a social preference for a year lived by a young adult over other ages there is economic logic to weighting young adults who are more economically active than children or older people. Age weighting has nevertheless been criticized because it is viewed as iniquitous and not based on empirical evidence[71]. Discounting in health is used to adjust for time differences[72], but this is also seen as controversial and unfair[73]. However, it is important to use discounting otherwise there is inconsistency in assessing the value of health outcomes in that costs are discounted whereas benefits are not[74]. Moreover if future health benefits are not discounted the implication is that the sum of all future health benefits is greater than the health of today's population so all available health care resources today should be directed towards tackling ill-health in future generations.[75].

The YLD data provided by WHO were in three formats: Standard DALYs (3% discounting with age weights), Discounted DALYs (3% discounting but no age weights) and No Frills DALYs (no discounting and no age weights). The 3% discount rate is recommended by U.S. Panel on Cost-Effectiveness on Health and Medicine, which also recommends performing a sensitivity

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[68] Colin D. Mathers C., Alan D. Lopez A. and Christopher J. L. Murray, C. (2006) Chapter 3: The Burden of Disease and Mortality by Condition: Data, Methods, and Results for 2001 in Global Burden of Disease and Risk Factors, Ed by Lopez, A., Mathers, C., Majid Ezzati M., Dean T. Jamison, D. and Christopher J. L. Murray, C. Pub by Oxford University Press and The World Bank http://www.dcp2.org/pubs/GBD

[69] http://books.google.ca/books?id=F8Abr-ofOwIC&pg=PA74&lpg=PA74&dq=how+is+disability+wieght+in+YLD+defined&source=bl&ots=5oJEs7Rl_x&sig=jHbSv473B4oB10cTR7BzPYIDGQI&hl=en&ei=Lb2eSumDIoWQsgPFpLke&sa=X&oi=book_result&ct=result&resnum=6#v=onepage&q=&f=false

[70] http://www.dcp2.org/pubs/GBD/5/Section/864

[71] Robberstad, B. (2005) QALYs vs DALYs vs LYs gained: What are the differences, and what difference do they make for health care priority setting? Norsk Epidemiologi 2005; 15 (2): 183-191

[72] Robberstad, B. (2005) QALYs vs DALYs vs LYs gained: What are the differences, and what difference do they make for health care priority setting? Norsk Epidemiologi 2005; 15 (2): 183-191

[73] Torgerson, D.; Raftery, J. (1999) Discounting *BMJ* 999; 319:914-915

[74] Smith, D.; Gravelle, H. (2000) The Practice of Discounting Economic Evaluation of Health Care Interventions http://www.york.ac.uk/inst/che/pdf/tp19.pdf

[75] http://www.dcp2.org/pubs/GBD/5/Section/864

analysis[76]. Ideally the age weighting should be incorporated into the model but since a format with age weighting but no discounting is not presented then the no frills DALYs were used for analysis to avoid double discounting since the data are subsequently discounted in the model developed here. Further it is possible to age-weight the no frills data (in terms of economic productivity) into the model[77].

The formula for the DALY is therefore expressed as follows[78]:

DALY = YLL + YLD

where $YLL(c,a,s) = N(c,a,s)$ x $L(a,s)$,
and where $N(c,a,s)$ is the number of deaths due to cause c for given age a and sex s and $L(a,s)$ is the standard loss function in years for age a and sex s.

where $YLD(c,a,s) = I(c,a,s)$ x $DW(c,a,s)$ x $L(c,a,s)$,
and where $I(c,a,s)$ is the number of incident cases for cause c, age a, and sex s; DW(c,a,s) is the disability weight for cause c, age a, and sex s; and $L(c,a,s)$ is the average duration in years of the case until remission or death.

Similar to the DALY, a QALY combines duration and quality of life[79]. The QALY is calculated by multiplying life expectancy by a quality of life weight (between 0 [death] and 1 [perfect health], the inverse of the disability weights used in YLD). The formula for the QALY is expressed as

QALY lived in one year = 1 x QALE

where QALE, the quality adjusted life expectancy is expressed as:

$$\mathrm{QALE} = \sum_{t=a}^{a+L} Q_t$$

[76] http://www.dcp2.org/pubs/GBD/5/Section/864
[77] Feyrer, J. (2002) Demographics and Productivity. Available at SSRN: http://ssrn.com/abstract=325365 or DOI: 10.2139/ssrn.325365
[78] Colin D. Mathers C., Alan D. Lopez A. and Christopher J. L. Murray, C. (2006) Chapter 3: The Burden of Disease and Mortality by Condition: Data, Methods, and Results for 2001 in Global Burden of Disease and Risk Factors, Ed by Lopez, A., Mathers, C., Majid Ezzati M., Dean T. Jamison, D. and Christopher J. L. Murray, C. Pub by Oxford University Press and The World Bank http://www.dcp2.org/pubs/GBD
[79] Sassi, F. (2006) Calculating QALYs, comparing QALY and DALY calculations. Health Policy and Planning. 2006 Sep; 21(5):402-8.

and where L is the residual life expectancy of the individual at age a, and t represents individual years within that life expectancy range[80]. The QALY, like the DALY, may be discounted or un-discounted.

The aim of these metrics is to enable policy makers to carry out a cost-utility analysis, informing decisions about the allocation of limited health care resources to achieve maximum benefit[81]. The differences in the methods used to calculate these metrics and the controversy about which, if either, is the more equitable[82,83] have briefly been outlined above but are not considered further for the purpose of model development. DALY data are more widely available hence this was used as the primary source of data in the model; however, to use QALY data in the model, the data can be entered as simply "1-QALY" instead of YLD so it is relatively straight forward to switch between either metric to do the cost effectiveness analysis.

To quantify the level of economic impairment caused by disease only the YLD data are required for the model. YLD for LF was divided into the prevalence data for the disease (itself estimated from prevalence in the total population) and the amount of YLD (in years) per worker (divided by 15 years – the life of the project) was then subtracted from the annual productivity of the healthy population to obtain the annual productivity of a worker with LF. This is shown in equations 1 to 3:

Total disability (YLD) per infected person (total population) = YLD/Prevalence (1)

Total disability (YLD) per infected person (working population) = (1) x Labour force participation rate (%) (2)

Annual disability (YLD) per infected person (working population) = (2)/15 years (3)

The difference between the value calculated for productivity with disease and productivity of the healthy population (described in 6.1) is the economic burden of disease (See Appendix I).

6.3 Costing the intervention

The third element required to build the model is the cost of interventions (usually drugs for NDs). For each disease type the appropriate treatment has to be identified and then costed. Reliable sources of drug prices were identified and the costing of the required treatments allowed

[80] Sassi, F. (2006) Calculating QALYs, comparing QALY and DALY calculations. Health Policy and Planning. 2006 Sep; 21(5):402-8.
[81] Dolan, P., Rebecca Shaw, R., Tsuchiyad, A. and Williams, A. (2005) QALY maximisation and people's preferences: a methodological review of the literature. Health Economics 14: 197–208 (2005)
[82] King, C. and Bertino, A. (2008) Asymmetries of Poverty: Why Global Burden of Disease Valuations Underestimate the Burden of Neglected Tropical Diseases. PLoS Neglected Tropical Diseases Mar 26, 2, 3: e209
[83] Sassi, F. (2006) Calculating QALYs, comparing QALY and DALY calculations. Health Policy and Planning. 2006 Sep; 21(5):402-8.

the NPV calculation showing the benefits (or otherwise) of intervention. The market for medicines is unique in a number of ways and is discussed further below (Section 7).

6.4 Creation of a data-sources database

A further output of the project is the compilation of data sources (for economic activity, for health related metrics and for pharmaceutical drug pricing) which were time consuming to identify. The creation of a database of sources will significantly improve efficiency in data mining and analysis for future projects (See Appendix III).

7. Pricing of Medicines

There are three commonly used pricing models:

1. Cost plus model where the product is priced to cover the variable and fixed costs of production as well as to provide a fair return,
2. Customer driven pricing where the price is based on what customers are willing to pay,
3. Competition driven pricing where products are priced competitively relative to competing products in order to win market share.[84]

In perfect markets a price equilibrium is established where marginal utility from consumption by consumers is equal to the marginal cost of production[85]. This is essentially a type of cost plus pricing. The market for medicines however is not perfectly competitive since on the consumption side demand does not reflect marginal utility because medicines are often purchased by agents on behalf of the patient (e.g. Doctors prescribing medicines, or medicines are approved by central technology assessment agencies such as the UK National Institute of Clinical Excellence which approve medicines that can be prescribed on the NHS on the basis of efficacy and cost effectiveness[86]) while on the production side prices are set considerably above the marginal cost of production. Pharmaceutical companies justify this type of monopolistic pricing[87,88], which has traditionally been used for introduction of new drugs by stating that the price of a new drug has to cover not only the production costs but also the R&D costs of business including the R&D costs for drugs which failed to reach market during the long and expensive development process[89]. These costs (incorporating the costs of failed projects and time costs)

[84] Nagle, T.T.; Hogan, J. E. (2005) Ch. 1 Tactical Pricing. In: The Strategy and Tactics of Pricing: A Guide to Growing More Profitably (4th Edition) Pub by Prentice Hall, 1-13

[85] Capri, S.; Levaggi, R. (2004) Drug Pricing in a Regulated Market.
Available at SSRN: http://ssrn.com/abstract=542202 or DOI: 10.2139/ssrn.542202

[86] http://en.wikipedia.org/wiki/National_Institute_for_Health_and_Clinical_Excellence

[87] Nagle, T.T.; Hogan, J. E. (2005) Ch. 1 Tactical Pricing. In: The Strategy and Tactics of Pricing: A Guide to Growing More Profitably (4th Edition) Pub by Prentice Hall, 1-13

[88] Constance, J. (2007) Ch. 2: Strategic Perspectives on Drug Pricing and Reimbursement.
In: A Guide to Drug Pricing and Reimbursement Ed: Constance, J., Pub by Kalorama Information, 7-18

[89] DiMasi J.A.; Hansen R.W.; Grabowski, H.G. (2003)

have variously been estimated from $800 million (2000 dollars)[90] to $1.2 billion (in 2005 dollars)[91] by DiMasi and coworkers and forecast at $2.2 billion in 2009 dollars by Bain[92] and the trend has been one of rising costs[93] (Fig. 3). DiMasi *et al.*[94] have also estimated the cost of R&D only by therapeutic category estimating $500 million capitalized costs (in 2000 dollars) for development of anti-infectives (relevant for NDs). Interestingly an NPV return of $2.2 billion was reported in the same paper on this R&D outlay for anti-infectives only (this NPV was just below the average [$2.4 billion] for all therapeutic categories investigated in the study). The issue of R&D costs is further complicated by asymmetry of information since these costs cannot be accurately observed by price regulators[95] or for that matter by customers; however, one report suggests that pharmaceutical firms price innovative medicines 20 to 100 times higher than the marginal cost of production[96].

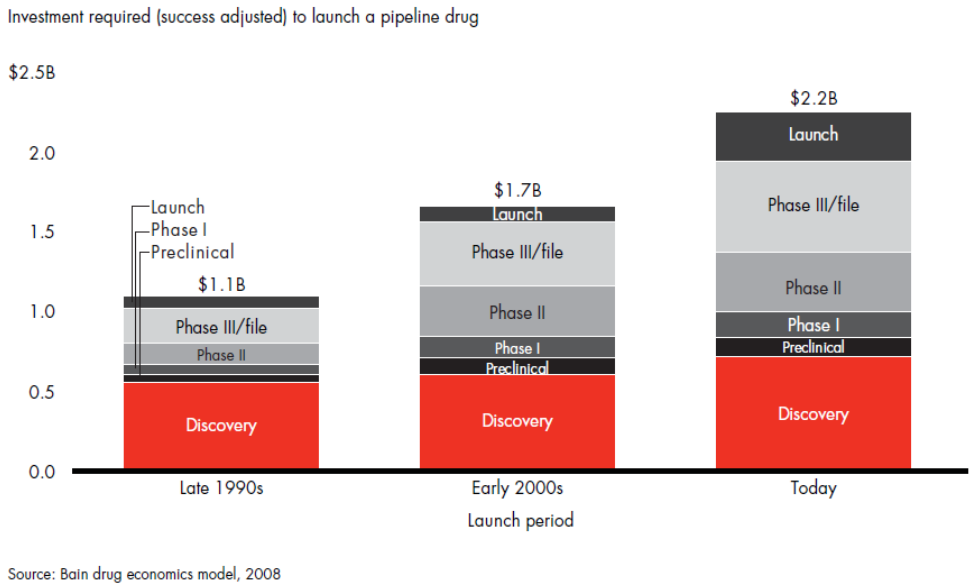

Figure 3 The rising costs of drug development (taken from O'Hagan, P.; Farkas, C., 2009).

In low- and middle-income countries 50% to 90% of medicines are paid for from "out of pocket" spending of patients and therefore the costs of medicines in these countries are beyond the reach

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The price of innovation: new estimates of drug development costs. Journal of Health Economics 22, 151–185

[90] DiMasi J.A.; Hansen R.W.; Grabowski, H.G. (2003)
The price of innovation: new estimates of drug development costs. Journal of Health Economics 22, 151–185.

[91] DiMasi J.A.; Grabowski, H.G. (2007)
The Cost of Biopharmaceutical R&D: Is Biotech Different? Managerial and Decision Economics 28: 469–479

[92] O'Hagan, P.; Farkas, C. (2009) Bringing pharma R&D back to health, Bain Brief, Pub by Bain and Company
http://www.bain.com/bainweb/PDFs/cms/Public/BB_Managing_RandD_HC.pdf

[93] O'Hagan, P.; Farkas, C. (2009) Bringing pharma R&D back to health, Bain Brief, Pub by Bain and Company
http://www.bain.com/bainweb/PDFs/cms/Public/BB_Managing_RandD_HC.pdf.

[94] DiMasi J.A.; Grabowski, H.G.; Vernon, J. (2007) R&D Costs and Returns by Therapeutic Category. Drug Information Journal, 38, 211–223

[95] Nagle, T.T.; Hogan, J. E. (2005) Ch. 1 Tactical Pricing. In: The Strategy and Tactics of Pricing: A Guide to Growing More Profitably (4th Edition) Pub by Prentice Hall, 1-13

[96] Constance, J. (2007) Ch. 2: Strategic Perspectives on Drug Pricing and Reimbursement. In: A Guide to Drug Pricing and Reimbursement Ed: Constance, J., Pub by Kalorama Information, 7-18

of many who require these medicines[97] (Fig. 4). This has led to pressure being exerted on pharmaceutical companies to reduce prices. In turn the pharmaceutical companies have developed a differential (discriminatory) pricing policy for different countries based on purchasing power, pricing medicines higher in high-income countries and lower in low- and middle-income countries[98]. In this way the pharmaceutical companies aim to recover most of their R&D costs from revenues generated in high income countries while reducing prices to just above marginal production costs in lower income countries. Although this appears to create a win-win scenario there are problems associated with this strategy. From the perspective of pharmaceutical companies there are two principal problems associated with differential pricing: first, parallel trade where medicines may be bought in low priced markets and shipped to higher priced markets and second, reference pricing policies, a pricing method used by national procurement agencies and national price regulators where the price of medicines is set based on prices charged in other national markets; setting prices lower in lower income countries may set a benchmark for regulators in high income countries to also ask for lower prices[99]. From the perspective of patients such a segmentation of the medicines market sets the interest of poor patients in different countries against each other rather than presenting a common front against the pharmaceutical companies[100].

The pricing of generic medicines follows a different model. The pricing model for these drugs is different since barriers to entry have largely been removed and pharmaceutical companies no longer enjoy the benefits of a monopoly, rather they face often intense competition, resulting in lower pricing[101]. In the U.S. market the introduction of legislation (Hatch-Waxman Act) resulted in the quicker introduction of generic drugs which sold at prices that were 50-60% of the brand name price resulting in rapidly increased market share for generics from 19% in 1984 to 43% in 1996[102]. More recently it has been reported that in the U.S. the price of a drug falls by 85% within one year of patent expiry because of generic competition[103]. The market for a drug is reported to segment upon entry of generic competitors into a price-sensitive segment and a brand-loyal segment. The generic manufacturers compete with each other in the price-sensitive segment, while the (newly) off-patent drug manufacturer focuses on the brand-loyal segment,

[97] WHO Policy Perspectives on Medicine No. 08, 2004 - Equitable Access to Essential Medicines: A Framework for Collective Action http://apps.who.int/medicinedocs/en/d/Js4962e/1.2.html

[98] Constance, J. (2007) Ch. 2: Strategic Perspectives on Drug Pricing and Reimbursement. In: A Guide to Drug Pricing and Reimbursement Ed: Constance, J., Pub by Kalorama Information, 7-18

[99] Constance, J. (2007) Ch. 2: Strategic Perspectives on Drug Pricing and Reimbursement. In: A Guide to Drug Pricing and Reimbursement Ed: Constance, J., Pub by Kalorama Information, 7-18

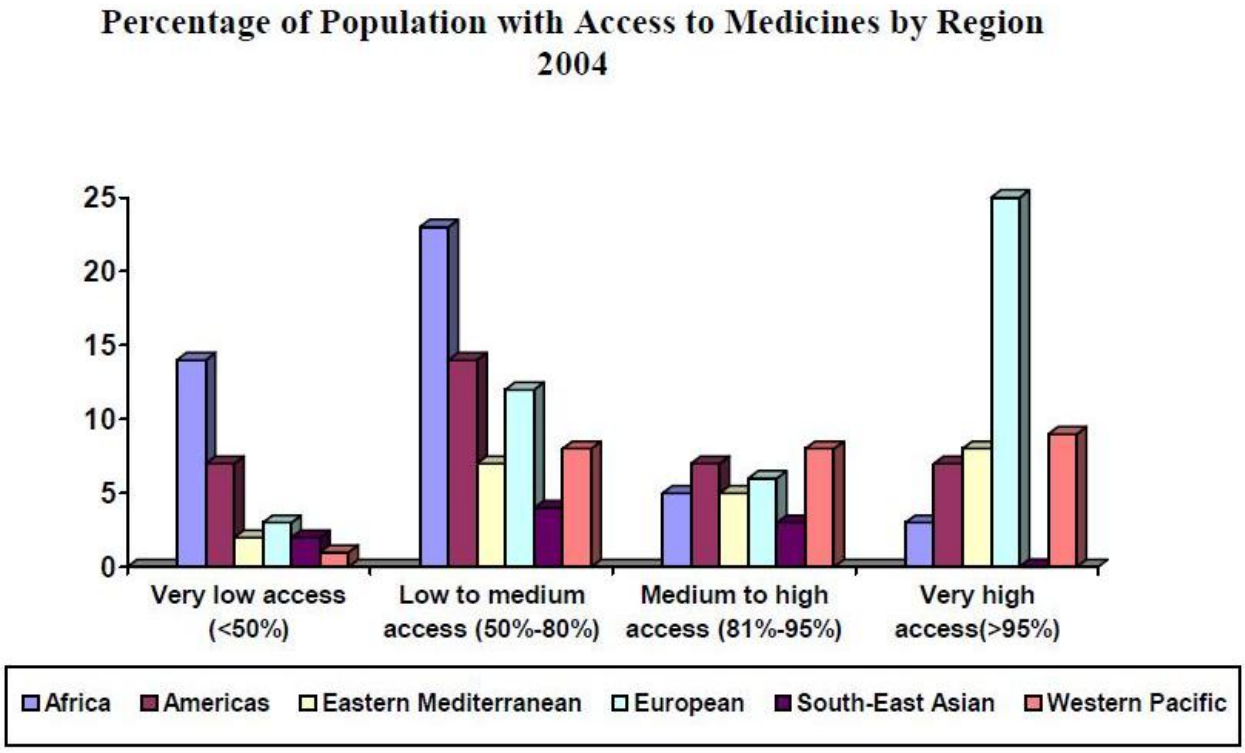
[100] Constance, J. (2007) Ch. 2: Strategic Perspectives on Drug Pricing and Reimbursement. In: A Guide to Drug Pricing and Reimbursement Ed: Constance, J., Pub by Kalorama Information, 7-18

[101] Löfgren, H. (2007) The global biopharma industry and the rise of Indian drug multinationals: implications for Australian generics policy. Australia and New Zealand Health Policy 2007, 4:10

[102] How Increased Competition from Generic Drugs has affected prices and returns in the Pharmaceutical Industry (1998) Congressional Budget Office Study. http://www.cbo.gov/doc.cfm?index=655

[103] Friends for life, The Economist, Aug 6th 2009 http://www.economist.com/businessfinance/displaystory.cfm?story_id=14177559

foregoing price-sensitive customers[104]. The competition between generics manufacturers reduces the price of the drug to a basic cost plus model. The price of generic medicines therefore more accurately reflect the costs of raw materials, production, supply and a fair return than the patented drug pricing model. It is however worth noting that although economic models predict that prices should decrease in the face of increased competition some newly off-patent drug prices have reportedly risen after the market entry of generics in what is called the "generic competition paradox". This is believed to be a response to the segmentation of the market, where a brand named manufacturer attempts to increase profits from brand-loyal customers[105,106].



Despite the difficulty in obtaining accurate price data[107] caused by the asymmetry of information mentioned earlier, the WHO along with Health Action International has attempted to create a database of prices for "essential medicines"[108] providing reliable information on the price of

[104] Regan, T. (2007) Generic entry, price competition, and market segmentation in the prescription drug market International Journal of Industrial Organization, 26, 930–948.
[105] Regan, T. (2007) Generic entry, price competition, and market segmentation in the prescription drug market International Journal of Industrial Organization, 26, 930–948.
[106] Scherer, F.M. (1993) Pricing, Profits, and Technological Progress in the Pharmaceutical Industry. Journal of Economic Perspectives, 7, 3, 97-115
[107] Kotwani, A. *et al.* (2007) Prices & availability of common medicines at six sites in India using a standard methodology Indian Journal of Medical Research 125, 645-654
[108] http://www.who.int/medicines/publications/08_ENGLISH_indexFINAL_EML15.pdf

medicines and enabling international comparisons of prices[109]. Essential medicines are defined by the WHO as those medicines "that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness."[110] Prices are obtained by surveying national procurement agencies and international medicines supply agencies[111]. The survey methodology developed by the WHO has also attempted to measure the price components in the supply chain; briefly, this is measured at five points along the chain which are common to all medicines:

Stage1: manufacturer's selling price + insurance and freight
Stage 2: landed price
Stage 3: wholesale selling price (private) or central medical stores price (public)
Stage 4: retail price (private) or dispensary price (public)
Stage 5: dispensed price[112]

The price survey goes into much greater detail of the factors which need be considered in determining the cost of each component; these factors include "manufacturer or importer prices, price differences arising from inter-country differences in import tariffs and non-tariff barriers, and differences in procurement costs, such as transport, delivery costs, wholesaling, domestic taxes and other mark-up costs which can differ considerably from one country to another."[113] The determination and analysis of price components by the WHO requires further investigation but for the purposes of the LF case study we will only examine the price data from the AFRO Essential Medicines Price Indicator publication[114] and the definitions used in that price list (Table 3).

Taking the LF example, the recommended treatment options are a one or twelve day treatment with diethylcarbamazine (DEC)[115] or a combination therapy of DEC and Ivermectin (in sub-Saharan Africa) or DEC an Albendazole elsewhere[116]. DEC, which inhibits metabolism of a cell membrane component[117], was first used as a microfilaricide in 1948[118] and is therefore assumed to be off-patent, Ivermectin, a neural inhibitor in worms[119], went off patent in 1996[120], while the

[109] Ch. 1: Introduction In Measuring medicine prices, availability, affordability and price components 2nd Edition Ed by Falvey, M. Pub by World Health Organization and Health Action International.
[110] http://www.who.int/topics/essential_medicines/en/
[111] http://www.who.int/medicines/publications/afro-essential_med_price_indicator_nocover.pdf
[112] Ch. 9: Measuring price components In Measuring medicine prices, availability, affordability and price components 2nd Edition Ed by Falvey, M. Pub by World Health Organization and Health Action International.
[113] Constance, J. (2007) Ch. 2: Strategic Perspectives on Drug Pricing and Reimbursement. In: A Guide to Drug Pricing and Reimbursement Ed: Constance, J., Pub by Kalorama Information, 7-18
[114] http://www.who.int/medicines/publications/afro-essential_med_price_indicator_nocover.pdf
[115] recommended by CDC http://www.cdc.gov/ncidod/dpd/parasites/lymphaticfilariasis/treatment_lymphatic_filar.htm
[116] Recommended by The Carter Center http://www.cartercenter.org/health/lf/index.html
[117] http://en.wikipedia.org/wiki/Diethylcarbamazine
[118] Duke B. O. L. (1972) Onchocerciasis. British Medical Bulletin 28, 1, 66-71
[119] http://en.wikipedia.org/wiki/Ivermectin
[120] http://beefmagazine.com/health/parasites/0401-dewormer-working/

patent on Albendazole, which inhibits energy metabolism[121], expires in 2013[122]. The prices for these medicines are shown in Table 4.

EXW	Ex Works	Seller delivers when he places the goods at the disposal of the buyer at the seller's premises or another named place (i.e. works, factory, warehouse etc.) not cleared for export and not loaded on any collecting vehicle.
FOB	Free on Board	Means that the seller delivers when the goods pass the ship's rail at the named port of shipment. This means that the buyer has to bear all cost and risks of loss or damage to the goods from that point. The FOB term requires the seller to clear the goods for export. *This term can be used only for sea or inland waterway transport.*
CFR	Cost and Freight	Means that the seller must pay the cost and freight necessary to bring the goods to the named port of destination. The risk of loss or damage to the goods after goods have passed the ship's rail in the port of shipment is transferred from the seller to the buyer. Consequently, the buyer will have to arrange the insurance. The CFR term requires the seller to clear the goods for export. *This term can be used only for sea and inland waterway transport.*
CIF	Cost, Insurance and Freight	This term has exactly the same conditions and obligations as CFR. However, in CIF the seller also has to procure marine insurance against the buyer's risk of loss or damage to the goods during carriage (transport) to the named port of destination. The CIF term requires the seller to clear the goods for export. *This term can be used only for sea and inland waterway transport.*
CIP	Cost and Insuranc e Paid	Means that the seller pays the cost of carriage necessary to bring the goods to the named destination. In addition the seller also has to procure insurance against the buyer's risk of loss or damage during carriage to the named place of destination. Consequently, the seller contracts the insurance and pays the insurance premium. The CIP term requires the seller to clear the goods for export. *This term may be used irrespective of the mode of transport, but is generally used for transport by air, rail and road.*
DDP	Delivery, Duty Paid	Means that the seller delivers the goods to the buyer, cleared for import, and not unloaded at the named place of destination. The seller has to bear all costs and risks involved in bringing the goods thereto including 'duty' for import in the country of destination. *This term may be used irrespective of the mode of transport.*

Table 3 Acronyms and definitions of terms of sale negotiated between manufacturers and customers for the WHO AFRO Medicine Price Indicator survey. "Whilst the EXW term represents the minimum obligation for the seller, DDP represents the maximum obligation." For example it is reasonable to add 20-30% for shipping costs to EXW or FOB prices whereas tender prices in CIF or DDP prices do not require adjustment for shipping prices[123].

The intervention (and prevention) options for early stage LF is a single or twelve day dose of DEC (6 mg/kg/day as recommended by CDC), given the data below this therapeutic option would cost at most (0.0083 cents x 12 tablets x 12 days) for a 100 kg patient giving a total cost of $1.195. A second option, recommended by the Carter Center, is a co-therapy of DEC and Albendazole the optimal dosage regimen has been found to be a single annual dose of

[121] http://en.wikipedia.org/wiki/Albendazole
[122] Expiry date: 15/9/2013 (http://www.locumusa.com/pdf/members/dop-100.pdf)
[123] http://www.who.int/medicines/publications/afro-essential_med_price_indicator_nocover.pdf

Albendazole (600 mg) plus a single annual dose of DEC (6 mg kg^{-1})[124]. This would cost at most (6.42 cents x 1.5 pills) + (0.0083 cents x 12 pills) for a 100 kg patient giving a total cost of $1.09. These prices should be well within the reach of the poor in India.

Medicine	*Data supplied by*	*Package*	*Pack Price (US$)*	*Unit Price (US$)*	*DDD*	*EML*	*Shelf Life*	*Stability*
DEC citrate 50 mg tablet (PO)	Action	7000 tab	20.6073	0.0029 EXW		E	3 yrs	Deg.
	IDA	1000 tab	3.4345	0.0034 EXW				
	ORBI	1000 tab	4.3275	0.0043 EXW				
	Cameroun	1000 tab	2.8507	0.0029 CIF	0.4 gm	E	3 yrs	Deg.
	Comores	1000 tab	5.633	0.0056 EXW	0.4 gm			
	Ethiopia	1000 tab	7.496	0.0075 DDP	0.4 gm			
	STP	1000 tab	3.46	0.0035 FOB	0.4 gm			
	Zambia	100 tab	0.83	0.0083 CIF/CIP	0.4 gm			
Albendazole 400 mg tablet (PO)	Ida	1000 tab	63.7845	0.0637 EXW	0.4 gm	E*		Stable
	Tri-Med	1000 tab	22.50	0.0225 FOB	0.4 gm			NA
	Comores	500 tab	26.2887	0.0526 EXW	0.4 gm			NA
		500 tab	15.3093	0.0306 EXW	0.4 gm			NA
	Gabon	100 tab	2.64	0.0264 DDP	0.4 gm			NA
	Mali	1000 tab	29.8104	0.0298 CIF	0.4 gm			NA
	STP	1000 tab	64.21	0.0642 FOB	0.4 gm			NA
	Togo	100 tab	5.371	0.0537 CIF	0.4 gm			NA
Ivermectin 6 mg tablet	Mission	100 tab	10.90	0.1090	12 mg			
	CRSS	100 tab	5.50	0.0550				

Table 4 Prices quoted for medicines required for the treatment of LF to the WHO AFRO Medicine Price Indicator survey. Ivermectin data was obtained from the International Price Indicator Guide[125] DDD: Defined daily dose, EML: Essential medicines list, STP: São Tomé and Príncipe, NA: Data not available.

[124] Ottesen, E.A.; Ismail, M.M.; Horton, J. (1999) The Role of Albendazole in Programmes to Eliminate Lymphatic Filariasis. Parasitology Today, 15, 9, 382-386

[125] http://erc.msh.org/dmpguide/resultsdetail.cfm?language=english&code=IV6T&s_year=2008&year=2008&str=6%2

This data (Tables 3 and 4) enables a comparison of shipping and supply costs to try and inform the portion of the price of medicines which are related to these obligations for the seller. Analysis (Table 5) shows that for DEC the average cost of DDP/CIF, the maximum obligation for the seller was 58% higher than the average cost of EXW/FOB (the minimum obligation). In the case of Albendazole the average cost of DDP/CIF was, unexpectedly, 22% lower than the average cost of EXW/FOB. The source of Ivermectin prices (a different database) did not indicate terms of sale therefore a comparison of shipping and supply costs could not be made. Comparison of the prices of on-patent and off-patented drugs showed that DEC (off-patent) was approximately 10 fold cheaper than Albendazole (on-patent). The price of Ivermectin was however, higher than Albendazole. Since the price of Ivermectin was obtained from a different database a direct comparison with the other two medicine prices may not produce reliable analysis[126].

Drug	*On-Patent*	*Source*	*Terms of sale*	*Unit price (US$)*	*Average*	*Terms of Sale Cost Difference (%)*	*Patent v Non-patent average*
DEC	No	Action	EXW	0.0029			0.0048
		IDA	EXW	0.0034			
		ORBI	EXW	0.0043			
		Comores	EXW	0.0056			
		STP	FOB	0.0035	0.00394		
		Cameroun	CIF	0.0029			
		Ethiopia	DDP	0.0075			
		Zambia	CIF/CIP	0.0083	0.006233	58.20642978	
Albendazole	Yes	IDA	EXW	0.0637			0.0429375
		Comores	EXW	0.0526			
		Comores	EXW	0.0306			
		Tri-Med	FOB	0.0225			
		STP	FOB	0.0642	0.04672		
		Gabon	DDP	0.0264			
		Mali	CIF	0.0298			
		Togo	CIF	0.0537	0.036633	-21.58961187	
Ivermectin	No	Mission	Not stated	0.109			
		CRSS	Not stated	0.055	0.082		

Table 5 Comparison of the costs of medicines. The average price for the lowest and highest terms of sale obligation by sellers is compared. The price of DEC (off-patent) is compared with Albendazole (on-patent).

0mg&desc=Ivermectin&pack=new&frm=TAB-CAP&rte=PO&class_code2=06.1.2.&supplement=&class_name=(06.1.2.)Antifilarials

[126] Ivermectin was not included in the AFRO Medicine Price Indicator survey therefore the data for Ivermectin was obtained from another WHO source which did not indicate the terms of sale negotiated; further it is not clear if the data was obtained from African countries or the nature of the markets where the data was obtained from.

However, the 10 fold price difference between the on-patent (Albendazole) and off-patent (DEC) drug may provide a clue as to why the price of Albendazole with DDP/CIF obligations was lower than the EXW/FOB obligations. Here, a differential pricing strategy may be employed by the Albendazole manufacturer to maximize profits in each market that it operates in. In order to determine if this is the reason behind the lower price for the higher obligation, the purchasing power of buyers (whether countries or NGOs) as well as the nature of health care regulations has to be determined.

For advanced stage LF where a hydrocele or lymphoedema has formed surgical intervention is an option and these costs were also identified (Table 13) but not incorporated into the model because no universal recommendations are made for surgical intervention for LF[127].

8. Analysis of the model

Forecast GDP data for India is shown in Table 6, while population and labour force growth forecasts and productivity per worker (forecast GDP divided by the forecast labour force) are shown in Table 7. The NPV of productivity of the healthy population over 15 years is shown in Table 8. Over the 15 year forecast period the average NPV per capita of a healthy individual was $43000, $37000 and $33000 USD at 3%, 5% and 7% discount rates respectively.

The estimated prevalence of LF in India is 29,355,000 amongst the total population,[128] while the YLD is 3,936,000. [129] The YLD per infected person is therefore 0.13. The prevalence and YLD figures are for the total population. Taking the labour force participation rate as 58% (approximation based on the historical and forecast figures in Table 14) the YLD per infected person in the labour force is 0.078. This is the life time YLD estimate; however, for the purposes of the model this is divided by the 15 year life time of the project to give a YLD per infected person in the labour force per annum of approximately 0.005 (coincidently 15 years happens to be a close approximation to the reported loss of 11 years of productive life caused by LF in India[130]). The amount of productivity lost per annum due to this level of disability is shown in Table 9 and the productivity of the labour force with LF is the productivity of the healthy population (calculated in Table 9) minus lost productivity. The NPV of the labour force with LF is shown in Table 10 with 3%, 5% and 7% discount rates.

127

http://books.google.ca/books?id=sH_YL0aXvkkC&pg=PA70&dq=filariasis+treatment+option#v=onepage&q=cookbook&f=false

128 http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html data obtained from 2004 Global Burden of Disease update – Prevalence GBD 1990 regions.xls spreadsheet

129 http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html data obtained from 2004 Global Burden of Disease update - No frills DALYs YLD GBD 1990 regions.xls spreadsheet

130 Ramaiah, K.; Das P. (2004) Mass Drug Administration to Eliminate Lymphatic Filariasis in India. *Trends in Parasitology* 20: 11 499 – 502.

Year	Forecast GDP (US$)
2007	1102351000000
2008	1209686000000
2009	1185726000000
2010	1234044000000
2011	1323243000000
2012	1441115000000
2013	1582120000000
2014	1739984000000
2015	1737320000000
2016	1822808000000
2017	1908296000000
2018	1993784000000
2019	2079272000000
2020	2164760000000
2021	2250248000000
2022	2335736000000
2023	2421224000000
2024	2506712000000

Table 6 India GDP forecast to 2024. The data from 2007 to 2014 are from the IMF. 2007 is actual GDP while 2008 to 2014 are IMF forecasted GDP figures. The data for 2015 to 2024 are forecasts using linear regression of the IMF figures (Appendix II, Figure 5).

The NPV productivity loss due to LF over the 15 year period compared to a healthy worker is shown in Table 11. In the best case scenario (7% discounting) the NPV loss due to LF is approximately $170. While with a 3% discount rate (recommended and used by WHO) the NPV loss is approximately $225. The NPV cost of the different chemotherapy regimens recommended either by the CDC or the Carter Center are shown in Table 12, with a high and low price analysis. Medicines discounted at 3%, would at most cost approximately $15 but the prevention of disease or cure of early stage LF would result in a net gain (healthy productivity minus medical expenses) of approximately $210. In the low cost scenario the combined NPV of the DEC/Albendazole regimen (as recommended by the Carter Center and others[131]) is approximately 90 cents (3% discount rate) – this is negligible compared to the productivity gain resulting from remaining free of LF. Taking the 7% discounting, at worst there is still a $158 gain from investing in $12 DEC to gain $170 of productivity.

[131] Ottesen, E.A.; Ismail, M.M.; Horton, J. (1999) The Role of Albendazole in Programmes to Eliminate Lymphatic Filariasis. Parasitology Today, 15, 9, 382-386

Year	Population aged 15+ ('000)	Labour Force 15+ (‘000)	Productivity (US$ per worker)
2007	794003	465037	2370.458695
2008	805684	470674	2570.114347
2009	821256	478873	2476.07612
2010	836828	487072	2533.596676
2011	852400	495271	2671.755463
2012	867972	503470	2862.365186
2013	883544	511669	3092.077105
2014	899116	519868	3346.972693
2015	914688	528067	3289.961312
2016	930260	536266	3399.07434
2017	945832	544465	3504.901141
2018	961404	552664	3607.587974
2019	976976	560863	3707.272542
2020	992548	569062	3804.084616
2021	1008120	577261	3898.146592
2022	1023692	585460	3989.57401
2023	1039264	593659	4078.476027
2024	1054836	601858	4164.955853

Table 7 Forecasted total population aged 15 and over and forecasted labour force (aged 15+). The productivity is calculated as the dividend of forecast GDP divided by forecast labour force. See Appendix II, Table 15 and Figs. 6 and 7.

Year		Scenario Analysis		
		Discount rate		
		3%	5%	7%
2009	0	2476.076	2476.076	2476.076
2010	1	2459.803	2412.949	2367.847
2011	2	2518.386	2423.361	2333.615
2012	3	2619.47	2472.619	2336.543
2013	4	2747.27	2543.859	2358.931
2014	5	2887.128	2622.441	2386.345
2015	6	2755.291	2455.02	2192.24
2016	7	2763.758	2415.659	2116.773
2017	8	2766.801	2372.255	2039.884
2018	9	2764.916	2325.483	1962.289
2019	10	2758.559	2275.944	1884.589
2020	11	2748.152	2224.169	1807.293
2021	12	2734.082	2170.634	1730.824
2022	13	2716.706	2115.756	1655.531
2023	14	2696.353	2059.908	1581.703
2024	15	2673.327	2003.415	1509.572
	NPV	43086.08	37369.55	32740.06

Table 8 15 year NPV of the productivity (US$) of the healthy population with 3, 5 and 7% discount factors.

Year	Lost Productivity	Productivity of Labour force with LF (US$)
2009	12.8373	2463.239
2010	13.13552	2520.461
2011	13.85181	2657.904
2012	14.84003	2847.525
2013	16.03098	3076.046
2014	17.35249	3329.62
2015	17.05692	3272.904
2016	17.62262	3381.452
2017	18.17128	3486.73
2018	18.70366	3588.884
2019	19.22048	3688.052
2020	19.72241	3784.362
2021	20.21007	3877.937
2022	20.68408	3968.89
2023	21.145	4057.331
2024	21.59336	4143.362

Table 9 Forecasted reduced productivity of labour force (compare with data in column 3 of Table 7).

Year		Scenario Analysis		
		Discount rate		
		3%	5%	7%
2009	0	2463.239	2463.239	2463.239
2010	1	2447.05	2400.439	2355.571
2011	2	2505.329	2410.797	2321.516
2012	3	2605.889	2459.799	2324.429
2013	4	2733.027	2530.671	2346.701
2014	5	2872.16	2608.845	2373.973
2015	6	2741.006	2442.292	2180.874
2016	7	2749.43	2403.135	2105.798
2017	8	2752.457	2359.956	2029.309
2018	9	2750.581	2313.427	1952.115
2019	10	2744.257	2264.144	1874.819
2020	11	2733.904	2212.638	1797.923
2021	12	2719.907	2159.38	1721.85
2022	13	2702.621	2104.787	1646.948
2023	14	2682.374	2049.228	1573.503
2024	15	2659.467	1993.028	1501.745
	NPV	42862.7	37175.8	32570.31

Table 10 15 year NPV of the productivity (US$) of the LF population with 3, 5 and 7% discount factors

	Discount rate		
	3%	5%	7%
$NPV_{healthy}$-$NPV_{ill\text{-}health}$	223.3812	193.7437	169.7419

Table 11 NPV loss due to LF at 3, 5% and 7%. This is calculated by subtracting the NPV for an LF sufferer from that for a healthy individual (*i.e.* subtracted respective NPVs from Table 10 from the corresponding NPVs from Table 8)..

	3%	5%	7%
DEC (high)	15.46342	13.60097	12.08098
DEC (low)	1.288618	1.133414	1.006748
DEC/Albendazole (high)	2.534541	2.229275	1.98014
DEC/Albendazole (low)	0.886895	0.780076	0.692898

Table 12 NPV of medicine prices – high price and low price scenario with discount rates used as before. Currency: USD

Govt. Hospital (US$)	Private Hospital (US$)
5.7	14.3
14.3	57.1

Table 13 Cost of hydrocele surgery in India (from Ramaiah *et al*.). In Ghana it was reported as $30-60 USD.[132]

The requirement for surgical intervention is somewhat more complex since with advanced stage disease the patient can be microfilaria free but hydrocele and lymphoedema will still persist. Surgery for hydrocele (hydrocelectomy) can improve work capacity as a study in Ghana has shown[133]. The cost of hydrocele surgery in India was reported by Ramaiah *et al*[134] and is shown in Table 13. The nature of each hydrocelectomy has to be determined on a case by case basis, therefore the cost of surgery has not been incorporated into the model, but both of these cost estimates suggest that one or two operations during the 15 year period will still return a positive NPV. Moreover if the patient participates in chemotherapy (s)he is unlikely to suffer new bouts of hydrocele. There are also surgical interventions available for lymphoedema[135,136] but costs could not be identified in the literature; moreover the latest medical thinking on lymphoedema (of the leg) treatment recommends emphasis on hygiene, antibiotic treatment for secondary bacterial infection of the affected area and physiotherapy. It has been suggested that

[132] Ahorlu, C.; Dunyo, S.; Asamoah, G.; Simonsen, P. (2001) Consequences of hydrocele and the benefits of hydrocelectomy: a qualitative study in lymphatic filariasis endemic communities on the coast of Ghana, Acta Tropica, 80, 3, 215-221

[133] Ahorlu, C.; Dunyo, S.; Asamoah, G.; Simonsen, P. (2001) Consequences of hydrocele and the benefits of hydrocelectomy: a qualitative study in lymphatic filariasis endemic communities on the coast of Ghana, Acta Tropica, 80, 3, 215-221

[134] Ramaiah , K.; Guyatt, H.; Ramu, K.; Vanamail, P.; Pani, S.; Das, P. (1999) Treatment costs and loss of work time to individuals with chronic lymphatic filariasis in rural communities in south India. Tropical Medicine and International Health, 4, 1 pp 19–25

[135] http://www.vascular.co.nz/lymphoedema.htm

[136] http://books.google.ca/books?id=sH_YL0aXvkkC&pg=PA162&lpg=PA162&dq=treatment+for+filariasis+lymphoedema&source=bl&ots=s70Oc8NKtq&sig=dpZAiC170dQ4GbjM1hkwNtyu-tc&hl=en&ei=8_GdSu--NpGysgPAw-0o&sa=X&oi=book_result&ct=result&resnum=5#v=onepage&q=treatment%20for%20filariasis%20lymphoedema&f=false

lymphoedema may even be reversible using this type of therapy.[137] Since the authors of this study suggest that there is no "cookbook" for treatment of lymphoedema this cost has not been estimated in the model.

9. Discussion

An economic model has been developed and presented for one of the major NDs using secondary data from easily accessible sources. A listing of sources of economic data, health related metrics and medicine price data has been created in order to ease and facilitate similar analyses for other diseases in the future. Further, LF, a major cause of disability, was used as a case study with the major symptoms, the required treatments and the economic impact (in terms of YLDs) identified. The prices for required medicines and surgical interventions were also obtained and in the case of medicine prices were incorporated into the model. Examination of the relationship between on-patent and off-patent medicines showed a 10-fold difference for the on-patent medicine. The cost of supplying DEC was approximately 40% higher with the highest obligation for the seller compared to the lowest obligation, but for Albendazole the cost for the highest obligations was less than the lower obligations. The investigation of medicine prices was limited to the three medicines used to treat LF in this study. To enable a comprehensive analysis of prices a larger sample is required than just these medicines therefore this is an area for further research. The economic analysis returned a positive NPV for chemotherapy to treat and prevent LF. Including the cost of surgery (at the lower end of the range of costs provided) will still return a positive NPV if a few procedures only are undertaken.

In order to establish the validity of the model a comparison of data produced by other workers follows. Ramaiah *et al*.[138], in a study of the effects of ADL episodes on economic activity, quote a WHO estimate of an annual economic loss of 1.5 billion USD (in 1997) to the Indian economy caused by acute and chronic LF. Using this figure and a prevalence figure of approximately 30 million LF sufferers equates to an annual loss of $50 USD per LF sufferer. This is about 4 times higher than the annual loss calculated from the model (in 2009, $13 USD). However, in the same paper the authors estimate from their primary research of acute episodes in Tamil Nadu, an impoverished region of India, where the average wage for a male agricultural worker or weaver (the two main industries in the area) is $0.7 USD per day, that during acute episodes 3.73 hours of economic activity is lost per day compared to healthy workers (during an acute episode a sufferer worked an average of 0.68 hours only). There were, on average, 1.8 episodes per patient per year each with a mean duration of 3.58 days per episode. This results in a loss of approximately 6 working days per patient per annum (equivalent to $4.2 USD per annum).

137 http://books.google.ca/books?id=sH_YL0aXvkkC&pg=PA70&dq=filariasis+treatment+option#v=onepage&q=cookbook&f=false

138 Ramaiah, K.D. Ramu, K; Guyatt, H.; Kumar, K.; Pani, S.; (1998) Direct and indirect costs of the acute form of lymphatic filariasis to households in rural areas of Tamil Nadu, south India. *Trop. Med. Int. Health* 3, 108–115

Assuming a 200 day work year this equates to a 3% loss of wages per patient. The loss of wages estimated from this study by Ramaiah *et al*. is 6-fold higher than the 0.5% lost productivity per annum estimated in the model. In this study sufferers spent on average $0.07 per treatment per patient, but of the patients that sought medical treatment (26.8% of sufferers only) their average spend was $0.92, 83% of which covered Doctors consultation fees and the cost of medicines. The ratio of money spent on treatments to lost wages is also higher than that calculated in the model ($1.67 USD on average spent per annum per patient seeking treatment, facing a loss of $4.2 per annum; this compares with a cost of less than a dollar spent on medicines to a loss of $13 of productivity in the model). This indicates that if the correct treatments are available at the prices costed in the model there is the demand to pay for treatments to cure LF especially if it can be cured before the disease advances to the chronic stage.

Another study[139] of the economic costs of the acute phase of the disease, in rural Orissa – another impoverished region of India, estimated the total loss of "potential working days" caused by acute LF only, at 0.09%. This estimate is less than the 0.5% used in the model, but the study examined acute cases only. The study found that each patient suffered 1.57 ADL episodes per annum each lasting on average 3.9 days resulting in approximately 6 days loss of work per annum. The average wage in this community was $1 (for men, $0.8 for women) resulting in an annual loss of $6 per male patient ($4.8 for female patients). This is approximately 46% of the lost productivity in the model ($13). Patients in this study spent an average of $1.20 per annum; however of those that sought treatment (65% of patients) the average spend increased to $1.85 per annum. The ratio of money spent on treatments to lost wages is also higher here than in the model – again potentially an indicator of willingness to pay for treatments.

Ramaiah *et al*. also investigated economic losses caused by chronic symptoms of disease[140], reporting a loss of 62 days of work per annum – equivalent to 17% of workdays (based on a 365 day working year) and 27% reduced productivity compared to healthy control patients. This is in comparison to a 0.5% reduced annual productivity incorporated into the model (combined acute and chronic LF burden). This reduced productivity is markedly higher than was obtained in the model by using the WHO prevalence and YLD data. The high productivity data obtained by Ramaiah and co-workers may be an anomaly nevertheless the disparity between the model data and the study data requires further investigation. Patients that sought and paid for treatment in this study (52%) spent an average of $2.1 USD per annum, 57% of which constituted Doctors fees while 23% constituted the cost of medicines – evidence of the ability of patients to pay for treatment. However since chronic LF (lymphoedema and/or hydrocele) requires either surgery or longer term physiotherapy then the costs of useful treatment may be beyond the patients investigated in this study.

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[139] Babu, B.; Nayak, A. (2003) Treatment costs and work time loss due to episodic adenolymphangitis in lymphatic filariasis patients in rural communities of Orissa, India Tropical Medicine and International Health 8, 12, 1102–1109

[140] Ramaiah , K.; Guyatt, H.; Ramu, K.; Vanamail, P.; Pani, S.; Das, P. (1999) Treatment costs and loss of work time to individuals with chronic lymphatic filariasis in rural communities in south India. Tropical Medicine and International Health, 4, 1 pp 19–25

In an examination of the benefits of a mass drug administration (MDA) program in India the authors[141] estimate the economic loss due to chronic LF at $39 USD per annum equivalent to a lifetime loss of $449 USD (including the cost of medication). The authors then cost the MDA program, one annual dose of DEC in Tamil Nadu, at $0.03-0.05 dependent on distribution and consumption rates (75% and 60% respectively) per capita in the district studied (or $0.2 per infected patient). This cost comprised of 61% of costs on medicines and 25% on personnel. (Interestingly extrapolation based on these medicine costs and economic loss caused by adverse reactions to medication was costed at $13.5 million USD for MDA treatment of the whole endemic population of India – a relatively low expenditure when considering the potential benefits of eradication of the disease from India as a whole). The paper calculates the life time cost of prevention (*i.e.* repeated annual doses) of one case of disease by DEC treatment at $8.41 USD. This gives a cost-benefit ratio of 0.019. The cost-benefit ratios in the model range between 0.07 (DEC high at 3% discount rate, see Table 12, and NPV at the same discount rate, Table 11) and 0.004 (DEC/Albendazole low at 3% discount rate and NPV at the same discount rate). This range is comparable to that reported in the study – a positive indication that the model produces good estimates of the cost-benefit ratio of treatments.

Finally, in a further paper reviewing research into the acute and chronic costs of LF Ramaiah *et al*.[142] estimated the total treatment costs and reduced working time costs associated with LF were approximately $842 million USD per annum to patients and households, equivalent to 0.63% of GNP. This is a figure which is consistent with the 0.5% annual GDP loss obtained from the model since the GNP is normally higher than GDP (net foreign income is additionally incorporated into the GNP data) and this paper incorporates the treatment costs as part of the economic loss.

In particular, this review of the economic costs associated with LF shows that the costs developed in this model are comparable to those estimated by other workers suggesting that the model can provide a good estimation of the real costs of disease and the benefits associated with treatment and cure of NDs. The range of medicine prices used in costing treatment are in good agreement with published data reviewed above. The costs associated with personnel delivering that treatment (after purchase of medicines) was not considered and this is an additional variable which can be incorporated into the pricing data to improve the accuracy of the costs of treatment.

The loss of economic productivity appears to be underestimated in this model in comparison with published data (e.g. 58 days of lost work per annum reported by Ramaiah and Das).[143] While it was a goal of the project to provide conservative estimates, identifying the sources of underestimation will help in the development of a more accurate model. One source of

[141] Ramaiah, K.; Das P. (2004) Mass Drug Administration to Eliminate Lymphatic Filariasis in India. *Trends in Parasitology* 20: 11 499 – 502.
[142] K.D. Ramaiah, P.K. Das, E. Michael and H. Guyatt (2000) The Economic Burden of Lymphatic Filariasis in India *Parasitology Today, 16, 6, 251-253*
[143] Ramaiah, K.; Das P. (2004) Mass Drug Administration to Eliminate Lymphatic Filariasis in India. *Trends in Parasitology* 20: 11 499 – 502.

underestimation is likely to be the prevalence and YLD data from the WHO. The WHO case definition for LF only includes cases of hydrocele greater than 15 cm or lymphoedema cases. Therefore the burden of disease caused by acute cases or hydrocele smaller than 15 cm is not incorporated into the data. There is now evidence to suggest that there is considerable burden of disease caused by LF prior to onset of hydrocele/lymphoedema; for example ADL is reported to be a significant cause of morbidity, while there is also evidence that the burden of extra-lymphatic disease caused by LF is more important than generally recognized because of diagnostic deficiencies.[144] The published studies examined at first hand the economic losses caused in endemic areas whereas the model presents losses based on data for the whole of India (including areas free from LF; this is a limitation of using data for whole countries, or whole regions) but is necessary for the development of a generic model. A further source of underestimation may be the treatment of the population data – the data presented in the model are non-age weighted for both economic productivity and disability (no frills YLDs); this was because of the complexity of assigning age weights to both economic activity and the burden of disease. An improved model should include this type of weighting to better reflect the economic burden of LF and disease in general. Since researchers have reported the average age of LF sufferers to be in the 40s[145,146] the model can be weighted to emphasize loss in particular age groups within the population and this may produce results which are in better agreement with published primary studies. The gender distribution of the workforce and the relative earning of males to females was also not considered in the model again because of the complexity of developing appropriate gender based weights. Since females earn less relative to men this may be a further source of under-estimation in the model as males were more likely to be infected[147] and also had higher earnings[148]. The introduction of gender based weights will improve the accuracy of the model.

It is also worthy to note that there are significant un-accounted for benefits to chemotherapy which are not incorporated into the model and which would reduce the relative cost of treatment. The medicines recommended for treatment of LF are wide spectrum agents which can prevent or eliminate other diseases, for example DEC is used for treatment of other filarial diseases including Loiasis[149], Albendazole is used in treatment of hookworm, tape worm and other nematode infections[150] and Ivermectin is used in treatment of onchocerciasis, a major cause of

[144] Engels D, Savioli L. (2006) Reconsidering the underestimated burden caused by neglected tropical diseases. Trend in Parasitology.22, 8, 363-6.
[145] Ramaiah, K.; Das P. (2004) Mass Drug Administration to Eliminate Lymphatic Filariasis in India. *Trends in Parasitology* 20: 11 499 – 502.
[146] Babu, B.; Nayak, A. (2003) Treatment costs and work time loss due to episodic adenolymphangitis in lymphatic filariasis patients in rural communities of Orissa, India Tropical Medicine and International Health 8, 12, 1102–1109
[147] Michael E, Bundy DA, Grenfell BT. (1996) Re-assessing the global prevalence and distribution of lymphatic filariasis. Parasitology. Apr;112:409-28
[148] *e.g.* Babu, B.; Nayak, A. (2003) Treatment costs and work time loss due to episodic adenolymphangitis in lymphatic filariasis patients in rural communities of Orissa, India Tropical Medicine and International Health 8, 12, 1102–1109
[149] http://en.wikipedia.org/wiki/Diethylcarbamazine
[150] http://en.wikipedia.org/wiki/Albendazole

disability amongst NDs[151]. Therefore the cost of this type of therapy should be balanced against not only the burden of disease caused by LF but also the other diseases that it can prevent or cure.

Despite some of the short comings of the model it appears that the data produced are within the range of data obtained from primary research in India. This type of field study is not only time-consuming, since the studies reviewed were over a period of at least one year but also costly. Therefore the main advantage of this model is that it readily enables the estimation of the costs and benefits associated with a treatment programme for diseases (not only NDs but all diseases for which DALY or QALY data are available). Further in the case of LF in India, the model, in agreement with other published analyses, appears to indicate that there is an economic case for the introduction of chemotherapy regimens using other financing and delivery mechanisms to the existing government or donor programs.

[151] http://en.wikipedia.org/wiki/Ivermectin

Appendices

Appendix I – Calculation Methods

GDP data was obtained from the IMF website for the forecasted period 2007-2014. The IMF data was extrapolated to 2024 using linear regression(Fig. 5).

Historical labour force data between 1993 and 2007 were obtained using the KILM database software and forecast to 2024 also using linear regression (Table 15 and Figs 6 and 7).

Productivity was calculated in terms of output (GDP) per worker since data for labour force hours worked was not available for India. This represented the productivity per worker per annum over the 15 year forecast period (Table 7).

The sum of the 15 year forecast period was discounted to an NPV using the 3% discount rate recommended by Disease Control Priorities Project[152]. NPV was also calculated using alternate discount rates of 5% and 7%[153].

Prevalence and YLD of disease data were obtained from the WHO[154]. YLD per infected person was calculated (YLD figure in years divided by prevalence i.e. the number of infected people in the total population).

The YLD per person figure was for the whole population (100%) so this was multiplied by the labour force participation rate (58%). The YLD is the total number of years the person suffers from disease from infection until cured or death. For the purposes of this model it was divided by 15 years as no data could be found regarding the annualized rates of infection or cure. This figure then corresponded to the amount of disability per worker per year over the 15 year period of the model.

Disability per worker per year was multiplied by the productivity of the healthy population to make an estimate of the productivity loss caused by disease for each year of the forecast. To obtain the productivity of LF sufferers the productivity loss was subtracted from the productivity of the healthy population.

The productivity of LF sufferers was also discounted to an NPV using 3%, 5% and 7% to make comparisons with the NPV of the healthy labour force. The differences are reported in Table 11.

[152] http://www.dcp2.org/pubs/GBD/5/Section/864
[153] Smith, D.; Gravelle, H. (2000) The Practice of Discounting Economic Evaluation of Health Care Interventions http://www.york.ac.uk/inst/che/pdf/tp19.pdf
[154] http://www.who.int/healthinfo/global_burden_disease/estimates_regional/en/index.html

The price of medicines were obtained from the AFRO Price of Medicines Indicator survey. The price factored in to the survey was the most expensive option, an analysis with the cheapest option (1 dose of DEC per annum) was also provided. The price of medicines were also discounted by 3%, 5% and 7%.

Appendix II – Supplementary data

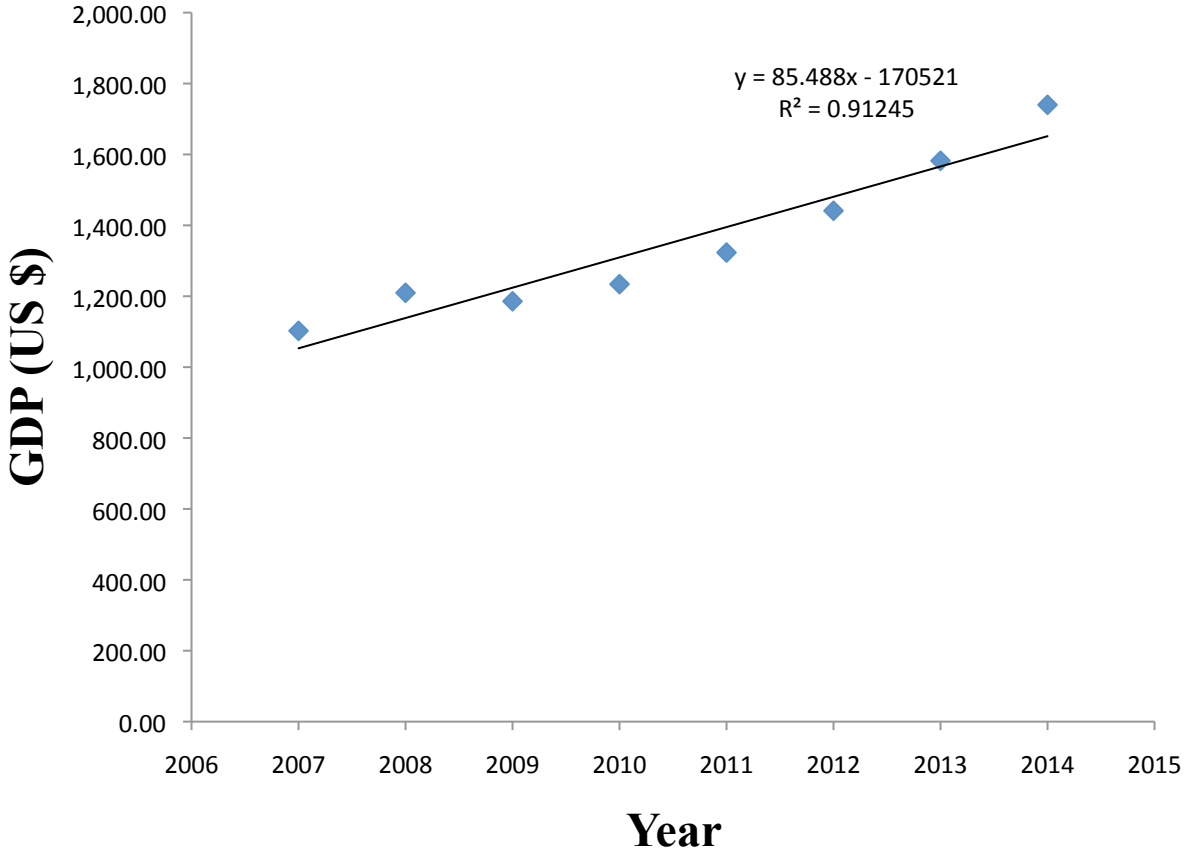

Figure 5 Linear regression of forecast GDP for India (2008 to 2014)

Year	Forecast GDP (US$)	Year on year growth (%)
2007	1102351000000	
2008	1209686000000	9.736917
2009	1185726000000	-1.98068
2010	1234044000000	4.074972
2011	1323243000000	7.228186
2012	1441115000000	8.907812
2013	1582120000000	9.784438
2014	1739984000000	9.978004

	Average	6.82%

Table 14 Average Year on year growth forecast for the Indian economy 2007-2014. The data is from IMF forecasts and gives an average annual growth rate of 6.82% - this was higher than the growth rates obtained from regression and therefore the regression growth forecast was used in the model.

Year	Population aged 15+ ('000)	Labour Force 15+ (‘000)	
1993	575974	349721	
1994	590131	357975	
1995	604552	365308	
1996	619238	372759	
1997	634179	380320	
1998	649345	387969	
1999	664700	395672	
2000	680217	403407	
2001	695865	411866	
2002	711644	420358	
2003	727598	428891	
2004	743792	437484	
2005	760260	447058	
2006	777013	457011	
2007	794003	465037	
2008	805684	470674	
2009	821256	478873	
2010	836828	487072	
2011	852400	495271	
2012	867972	503470	
2013	883544	511669	
2014	899116	519868	
2015	914688	528067	
2016	930260	536266	
2017	945832	544465	
2018	961404	552664	
2019	976976	560863	
2020	992548	569062	
2021	1008120	577261	
2022	1023692	585460	
2023	1039264	593659	
2024	1054836	601858	

Table 15 Historical data (1993-2007) used for Population and labour force growth forecasts (2008-2024).

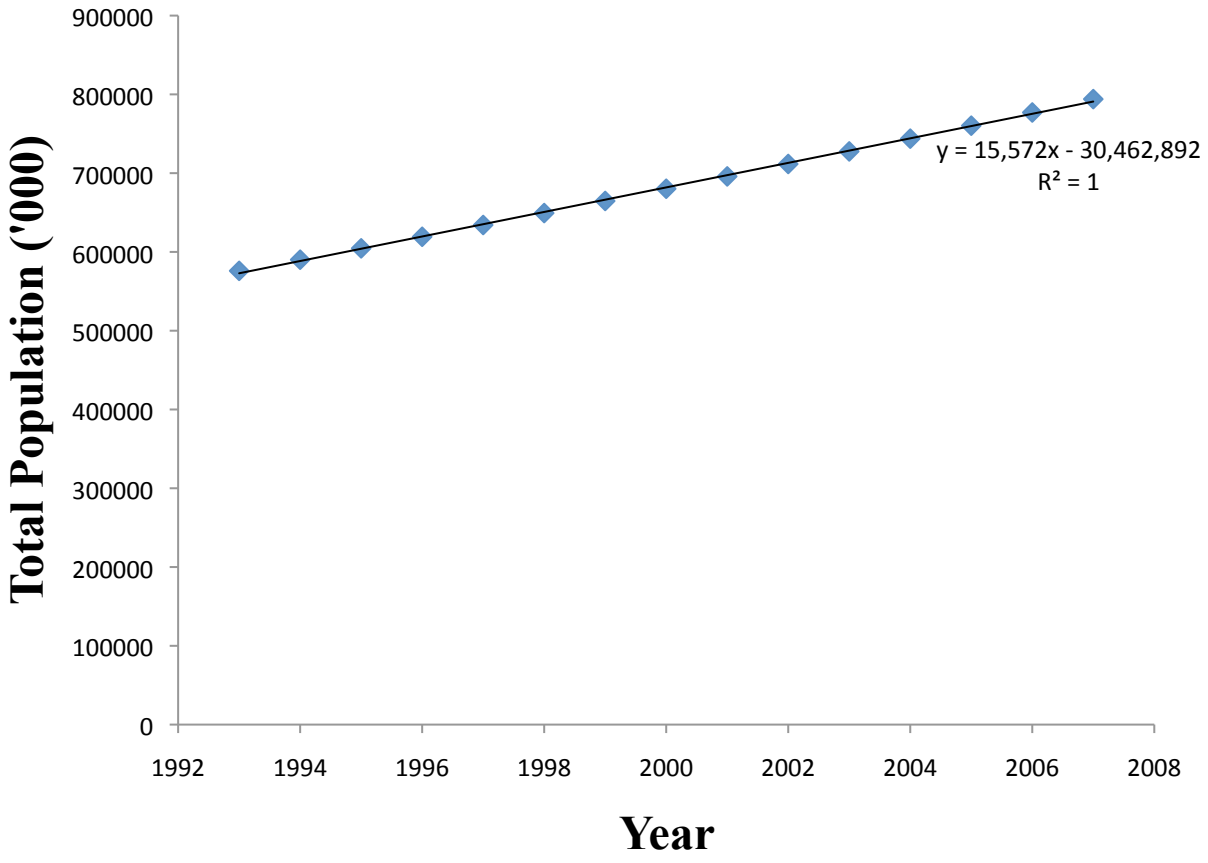

Figure 6 Linear regression for total Indian population growth from 1993 to 2007.

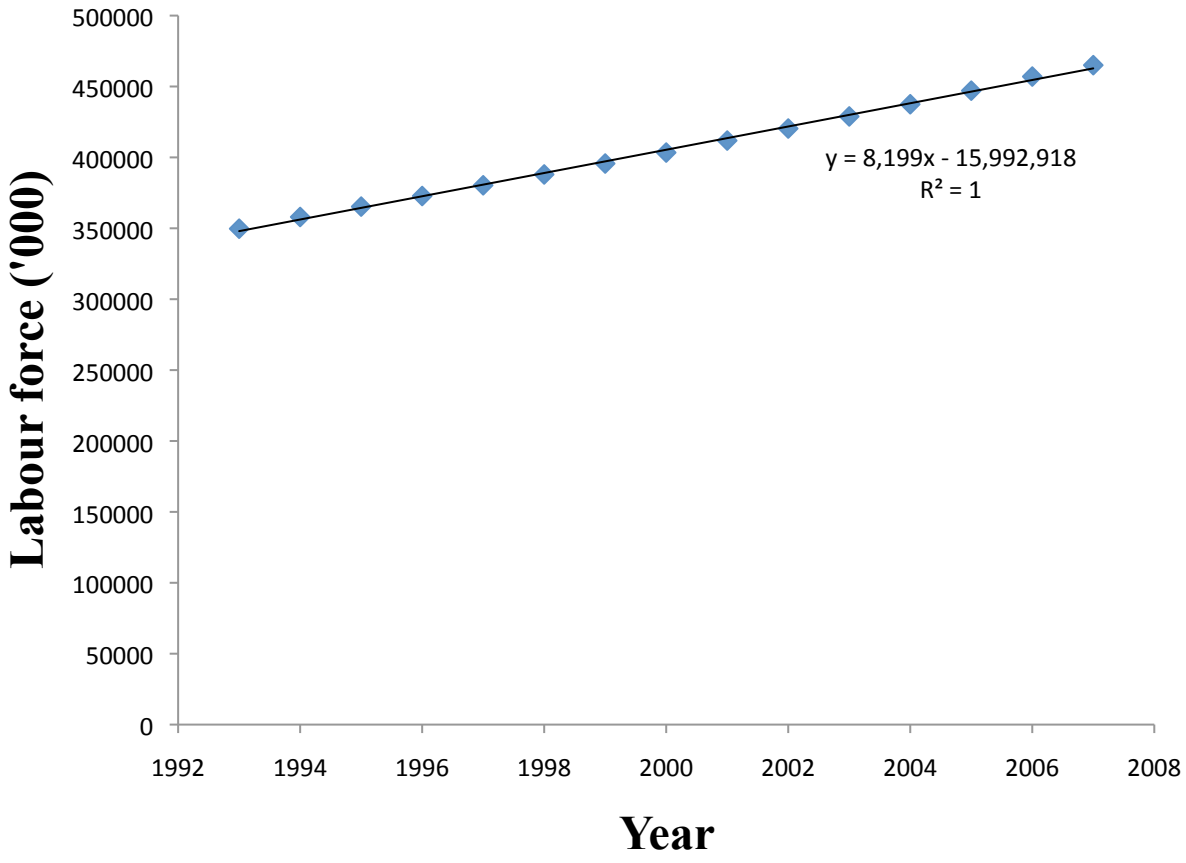

Figure 7 Linear regression for Indian labour force growth from 1993 to 2007.

Appendix III – Useful Data Sources

Economic Data

1. IMF at http://www.imf.org/external/pubs/ft/weo/2009/01/weodata/weoselgr.aspx8; http://www.imf.org/external/pubs/ft/weo/2009/01/weodata/index.aspx

2. The Groningen Growth and Development Centre – Six databases run by the University of Groningen comparing economic performance and growth rates at http://www.ggdc.net/

3. World Bank – an online database for numerous (approximately 26) social, political and economic statistics searchable online at http://econ.worldbank.org/WBSITE/EXTERNAL/EXTDEC/0,,menuPK:476823~pagePK:64165236~piPK:64165141~theSitePK:469372,00.html; OR http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20535285~menuPK:1192694~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html; http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20399244~menuPK:1504474~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html – explanation of difference between GDPs.
4. World Bank Country historical data at http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20535285~menuPK:1192694~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html
5. CIA World Fact book – however this site does not have forecasted GDP data https://www.cia.gov/library/publications/the-world-factbook/fields/2001.html?countryName=World&countryCode=XX&regionCode=oc&#XX ;

   limited to regional forecasts (by geography or by income) forecasts for three years (09-11): http://web.worldbank.org/WBSITE/EXTERNAL/EXTDEC/EXTDECPROSPECTS/EXTGBLPROSPECTSAPRIL/0,,menuPK:659178~pagePK:64218926~piPK:64218953~theSitePK:659149,00.html

   CIA: uses PPP but gives point estimates usually for the current/previous year
6. Penn World Tables – produced by the Center for International Comparisons of Production, Income and Prices produces PPP and national income accounts for 188 countries from 1950-2004 at http://pwt.econ.upenn.edu/

7. Key Indicators of the Labour Market – software database at http://www.ilo.org/public/english/employment/strat/kilm/

8. The International Labour Organization (ILO) database of labour statistics: http://laborsta.ilo.org/
9. UNIDO – Provides a number of free and for sale publications related to (industrial) productivity - http://www.unido.org/

Health metrics

1. Disease and injury estimates (BOD, HALE, LE) http://www.who.int/healthinfo/global_burden_disease/estimates_country/en/index.html
2. 14. Global Burden of Disease http://www.who.int/healthinfo/global_burden_disease/en/
3. 15. Online source of treatments for NDs: http://www.cdc.gov/DiseasesConditions/az/a.html

Cost of medicines

1. http://www.library.hbs.edu/cgi-bin/faq/recordDetail?action=&id=28374&institution=Penn&library=harvard_business
2. http://www.who.int/medicines/areas/access/ecofin/en/
3. http://erc.msh.org/mainpage.cfm?file=1.0.htm&id=1&temptitle=Introduction&module=DMP&language=English
4. http://www.haiweb.org/medicineprices/
5. http://aapredbook.aappublications.org/ - may need ubc login
6. http://www.micromedex.com/products/redbook/
7. http://www.micromedex.com/products/redbook/readyprice/

General

http://www.nationmaster.com/index.php - a website that collects comparative country data from numerous sources, you can then select the required outputs and can also use the site to generate graphs

http://www.oanda.com/convert/fxhistory - is a site that gives interbank exchange rates as recommended by AFRO medicine pricing indicator.

Journals

Public Library of Science Neglected Tropical Diseases

PharmacoEconomics: http://www.ingentaconnect.com/content/adis/pec

Value in Health: http://www.ispor.org/valueinhealth_index.asp - subscription required

Health Care Analysis