Health economic analysis of pharmaceutical inventory levels

Peter Benjamin Ellison
Department of Finance and Administration, World Health Organization, Western Pacific Regional Office, Manila, Philippines, and
Robert A. Cook
Management and Marketing, Northeastern Illinois University, Chicago, Illinois, USA

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Abstract

Purpose – Humanitarian crises increase vulnerability of children to pneumonia, so aid agencies store pharmaceuticals in advance of this demand. Decisions on how much to store are plagued by many diverse challenges as is common in humanitarian contexts, so this study considers storing more medications to improve the relatively poor (~80) demand coverage at a representative aid agency.

Design/methodology/approach – The paper combines inventory theory with health economics to calculate the impact inventory increases would have on the final cost of pneumonia treatment. It can then assess to what extent inventory can be increased while pneumonia treatment remains cost effective.

Findings – The study finds that more drug investment has only a small effect on the final treatment cost. Substantial drug inventory increases remain well within established guidelines for highly cost-effective treatments, so the agency should consider large increases as an efficient use of funding.

Research limitations/implications – The study focuses on pneumonia treatment only to allow sufficient depth of analysis. Further research could look at many other treatments using the same approach, although some problem scenarios will include complicating parameters like drug perishability.

Practical implications – The level of pharmaceutical inventory at humanitarian warehouses is a high-value decision for the aid sector. The method shows the potential for health economics to provide practical decision support for a wide range of humanitarian and ministry of health warehouse operations. While large increases in inventory investment are within guidelines, there is an asymptotically increasing cost as demand coverage approaches 100%. As a result, decision makers may want to set a target demand coverage (e.g. 99%) and allocate remaining aid funding to other projects.

Originality/value – Many humanitarian supply chain decisions lack analytical support due to issues with complexity, scale or a lack of reliable input data, and this study is the first to provide analytical insights which can greatly improve the current approach to inventory control policies for pneumonia medications and beyond.

Keywords Humanitarian logistics, Disaster relief operations, Pharmaceutical inventory, Risk management

Paper type Research paper

1. Introduction

Pneumonia claims the lives of an estimated 2m children under the age of five every year (Bryce *et al.*, 2005). Children are particularly vulnerable to pneumonia during humanitarian crises as these incidents lead to overcrowding, malnutrition and higher rates of other diseases, which in turn increase the risk of falling ill. Fortunately, pneumonia can be treated with low-cost drugs (World Health Organization, 2014) but only if the responding agency has a large enough stockpile of appropriate pharmaceuticals to meet the surge in demand. Aid budgets are limited, and managers are responsible for allocating the available funds in the most efficient way possible, so this begs the question, should these organizations store more medications to help meet the demand? This study seeks to answer this question by considering pharmaceutical inventory decisions at the warehouse of a child-focused aid agency which regularly provides aid to crisis areas.

The size and timing of sudden-onset events is unpredictable (Zeimpekis *et al.*, 2014); the requirements for pneumonia drugs cannot be known in advance, and aid agencies must have stockpiles in place to meet any demand that may arise. The reason for these to be bigger is clear: the more drugs that are stored, the more pneumonia cases can be treated during a large

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crisis. On the other hand, drug storage has a cost. Spending on warehouse storage can be high – perhaps already too high, tying money up in inventory to cover very unlikely contingencies, and that money might be better spent elsewhere. So how should the agency decide when they have the right level of stock?

The amounts of money involved are large. To give an idea, the values of total inventory stored at a few agencies are given below. Agency financial reports show that in 2016:

(1) International Committee of the Red Cross stored 72.8m USD (International Committee of the Red Cross, 2016)

(2) Médecins Sans Frontières (MSF) stored 57.5m USD (MSF, 2016)

(3) UNICEF stored 55m USD (UNICEF, 2016)

Across hundreds of aid agencies, humanitarian inventory is a major investment decision, so balancing costs and benefits is crucial. In practice, attempts to work out the right inventory level are undermined by the lack of decision support – and new forms of quantitative guidance are needed.

The difficulties are illustrated by contrasting the humanitarian and commercial/for-profit contexts. Money-making businesses, unlike humanitarian operations, have a clear cost/benefit guidance: they must stay within the limits of profit. As commercial warehouses start to increase inventory, they will benefit from more profit – that is, at first, the more inventory stored, the less often they run out when busy, and so fewer sales opportunities are missed, resulting in more profit. However, there will come a point when further increases are no longer profitable as there are insufficient spikes in demand to justify the amount of stored inventory. That is to say, any extra sales earned by the increase in inventory are not frequent enough to cover the higher storage cost. Calculating this point where inventory increases stop making profit is the basis for inventory decisions in commerce.

However, aid agencies must perform a more difficult calculation since the two sides of the cost / benefit equations are now in different terms; the costs of inventory investment are still in USD, but there is no USD profit. Instead, the profit (often called the benefit or utility instead) is measured in health or other service-based performance metric (Zeimpekis *et al.*, 2014). Increasing inventory will hopefully contribute to the preservation of life but will incur a financial cost either way; the additional inventory will cover increasingly infrequent crises, so further increasing the stock will have diminishing benefits even though the costs of storing each additional unit is the same [1]. Eventually, the next unit of inventory will add so much to the cost of pneumonia drugs that treatment is no longer cost-effective. In the aid sector, this inefficiency is even more detrimental as any increase in spending on inventory reduces the resources available for other humanitarian interventions, so decision makers must seek the optimal inventory level where the agency is not overinvesting or underinvesting.

Unfortunately, humanitarian logistics/disaster management (HL/DM) contexts introduce new sources of uncertainty and stochasticity which prohibit decision makers from simply combining conventional theory from supply chain management and health economics (several papers have thoroughly established these differences, such as Beamon, 2004; Van Wassenhove, 2006; Holguín-Veras *et al.*, 2007). Fortunately, a growing body of literature has arisen to provide decision support for diverse inventory control problems in HL/DM contexts that attempts to overcome these obstacles and solve these (in the words of Altay and Green, 2006) "large, intractable problems". The interested reader can supplement the discussion below by referring to one of several literature reviews that have been published on the topic in the last few years, such as Balçik *et al.* (2016), Leiras *et al.* (2014) or Galindo and Batta (2013).

Generally speaking, research specific to HL/DM contexts attempts to provide methodological adaptations to for-profit inventory control models that overcome the additional challenges specific to whatever humanitarian problem setting they address; however, these papers often make compromises in the name of tractability, either by requiring many and/or restrictive assumptions, limiting the scope of the problem setting, or both. This is especially true for papers attempting to find analytical solutions (e.g. Cook and Lodree, 2017), but even those employing simulation methods often restrict themselves to unrealistically small problems. For example, Lodree *et al.* (2017) consider a medical facility with at most six patients and three volunteer workers arriving in a given decision period. In contrast to these examples, fewer compromises can be made if using optimization software, but it may not be reasonable to assume a decision maker in the field would have access to potentially expensive software and possess the necessary technical background to use it. To make matters worse, these solvers often take more than a few minutes to find solutions (Tofighi *et al.*, 2016, for example, required over four hours to find a solution in each run of their MILP solver) which makes them unsuitable for use in the period immediately following a disaster (called the postdisaster phase). Comfort *et al.* (2004) explains how fragile the interconnected systems are that provide services to a community, and rapid response to a disaster is necessary to reverse the "cascading failure" of the socialtechnical network. Even when the timeliness issue is manageable – e.g. for studies in a pre-disaster context – it may be difficult to determine accurate parameter values to serve as inputs in the model (Tofighi *et al.*, 2016). Even the demand coverage value this study will use as a baseline could not be measured in a less well-run supply chain network, which unfortunately describes many in operation today as managers often lack some combination of training and financial or time resources necessary to develop their supply chain.

So, this suggests that in a perfect world agency managers would determine the amount of inventory to maintain by following simple, communicable insights that apply to a variety of situations without parametric sensitivity. While this may sound like a fanciful dream, this study will attempt to demonstrate the solution to the pharmaceutical stocking level problem described above may not be as complicated as it seems.

2. Vocabulary and concepts

There are two intended audiences for this work as follows: (1) humanitarian supply chain managers tasked with deciding on inventory levels but needing specialist concepts from health economics to make efficient decisions and (2) public health decision makers. The method described below shows how combining health economics with supply chain theory can allow aid agencies to compare the worth of inventory increases to other uses of funding.

The concepts used from each field are already well established, the novelty is in combining the two. Since the two intended audiences of this work may not be familiar with the other's vocabulary (i.e. supply chain managers may not be familiar with health economics and vice versa), it is worthwhile to summarize the key ideas used from both subjects, beginning with the vocabulary from supply chain management.

2.1 Concepts relating to supply chain management/cost inventory

Once combined, the supply chains concepts described in Section 2.1 can show the impact on the cost of a packet of drugs by finding the inventory value at the different percentages of demand coverage, working out what percentage of inventory value was spent on storage costs, giving a USD storage cost for the year which can be added to the annual USD throughput and showing how much more expensive it would be to store in increased quantities in order to cover greater percentages of emergency demand.

2.1.1 Demand coverage. Demand coverage is expressed as a percentage, indicating the proportion of demand that is satisfied and what demand is not met. For example, a demand coverage of 80% indicates that 80 units are satisfied out of every 100 units of demand. The more funds invested in inventory, the more product is available, and so more demand can be covered; for the purposes of this study, this means that additional funding spent on pharmaceuticals leads to more cases of pneumonia cured.

To be clear, this study is not talking about all global pneumonia outbreaks – the humanitarian demand far outstrips the donor funding – this paper discusses only the demand for which a particular aid agency has funding. The point of this paper is that there are times when aid agencies with more than enough funding still provide poor demand coverage because they do not carry enough stock. These agencies worry that overinvesting in inventory is a waste of funding, but they are as a result unprepared for large demand spikes when they occur (in fairness, it is reasonable to be concerned about waste as donors' perception of an organization's efficiency with funding is a key determinant of giving behavior Sargeant *et al.*, 2004). In the aid agency studied in this paper, the demand coverage for pneumonia drugs was about 80%, so about 20% of donor-funded, sudden demand due to outbreaks of pneumonia could not be met from the warehouse. To consider what might have been done, the cost of increasing demand coverage from 80% up to 99% was calculated.

2.1.2 Inventory value. For each increase in the percentage of demand coverage, there must be a corresponding increase in investment in inventory, so agencies should be interested in the average amount of funds tied up in inventory over the course of a financial year.

2.1.3 Storage costs. Storage costs are expressed as a percentage of the inventory value. Medication must be purchased to treat the disease, no matter the logistical circumstances, so the interest is in the cost of storing drugs, not drug inventory value itself. That is to say, whether an aid agency has one packet of drugs in the warehouse or 1,000 packets, the price originally paid for each packet purchased is not increasing. But if there is no extra purchase cost per packet, why not just buy huge amounts and cover all possible demand? After all, there is no extra purchase cost per packet, even big disasters could be covered, and all packets would get used eventually since the required medications for pneumonia have a long shelf life. However, there is still an increased cost as having enough drugs stockpiled to cover a crisis of larger/rarer magnitude means having more drugs and using them less often. As a consequence, higher storage costs are incurred as more space must be rented, more people are needed to manage the stockpile, more medication will expire and more money could otherwise have been earning interest in the bank or used for another purpose (i.e. opportunity cost). These storage costs are calculated as a percentage of average inventory value and expressed in USD per year.

2.1.4 Throughput. The throughput is the value in USD of drugs dispatched by the warehouse to emergencies, expressed as a yearly rate. It coincides with demand coverage and is used in calculations to see how storage adds to the cost of each packet of drugs dispatched. Throughput is generally higher than the average inventory because the warehouse will send and receive more units over the course of a year than they keep on hand at any given time. For example, consider a year in which the warehouse might start with 0 packets, receive 1,000 packets, send that 1,000 to an emergency, receive another 1,000 and send that 1,000 as well. In this case, they have sent 2,000 packets but never stored more than 1,000 at a given time.

2.2 Concepts relating to health economics

The remaining vocabulary terms are necessary to apply the concepts from Section 2.1 in a medical context.

2.2.1 Treatment costs. As storage costs increase, each packet of drugs becomes more expensive and so the cost of treating a disease goes up. Before the new cost can be calculated, it is necessary to know how much it costs to treat a disease without considering the additional complications of a humanitarian setting. In this paper, the baseline cost is the cost to the country's ministry of health – again, the amount paid without emergencies – which requires the same types of drugs that are stored at aid agency warehouses.

There are many baseline inputs alongside the drugs such as medical staff and hospital infrastructure, which can be gathered together to estimate the baseline treatment cost for a single episode of a disease.

2.2.2 Cost-effectiveness ratio. Once the costs are quantified, it is necessary to quantify the benefits of treating a pneumonia case. This gives a ratio of cost to benefit. The benefits are, roughly speaking, (see details below) lives saved, so the cost effectiveness ratio (CER) is how many USD it costs to save a life. More demand coverage makes the drugs more expensive, but the benefits of treatment remain the same, so the CER worsens.

2.2.3 Cost-effectiveness threshold. Aid money is constrained and must go as far as possible; maximizing the value for money is essential. Health economists have established cost-effectiveness thresholds which give guidance on when the amount spent per life saved – CER – has worsened to the point it is no longer good value.

Overall, the combination of supply chain and health economics can answer the question of if, and to what extent, the aid agency could store more pneumonia drugs without threatening good value treatments. Each step is covered in more detail below.

3. Methods

The research methodology employed in this study involves many steps, so the reader may find benefit in consulting the summative flow chart in Figure 1 while reading this section.

3.1 Demand coverage

The World Health Organization (WHO) standard treatment guidelines for pneumonia (WHO, 2014) require three drugs: amoxicillin, ampicillin and gentamicin. The three drugs underwent demand coverage analysis, starting with the current 80% demand coverage, up to 99% of donor-funded emergency demand.

To calculate the costs of increasing coverage, two sets of historical data are required:

(1) The demand history (all orders for the three pneumonia drugs)

(2) The history of how long it took suppliers to deliver pneumonia drugs (known as the lead time)

The aid agency covers crises large and small on a global basis, 24/7, often concurrently. The demand history shows how busy the agency was and how much pneumonia drug inventory would have been needed to cover the busiest times of the year. It is also necessary to know how often the supplier is late with their delivery because even when not that busy, drugs are needed to protect against running out if an inventory replenishment delivery is late. And clearly, if there is a busy period at the same time a supplier is late with their delivery, then very large quantities are required to meet demand while waiting for the late supplier.

This historical analysis can show how much inventory would have been needed to reach 99% demand coverage and thus provides a reliable guide to future requirements, assuming historical demand patterns remain relatively constant going forward. For the prediction to be useful, the historical trend must be flat, and demand and lead time distributions must be approximately normal. It is also necessary to review a long enough past record; five years of history is regarded as adequate in industry.

Records at the aid agency going back 5 years were extracted from co-operate databases and examined, ruling out linear trend and confirming normal distributions.

The next step was to input the raw data into a standard supply chain formula to calculate inventory levels required for increasing percentages of demand coverage. The formula is shown in Appendix 1, and resultant tabulation of inventory value is given in Appendix 2.

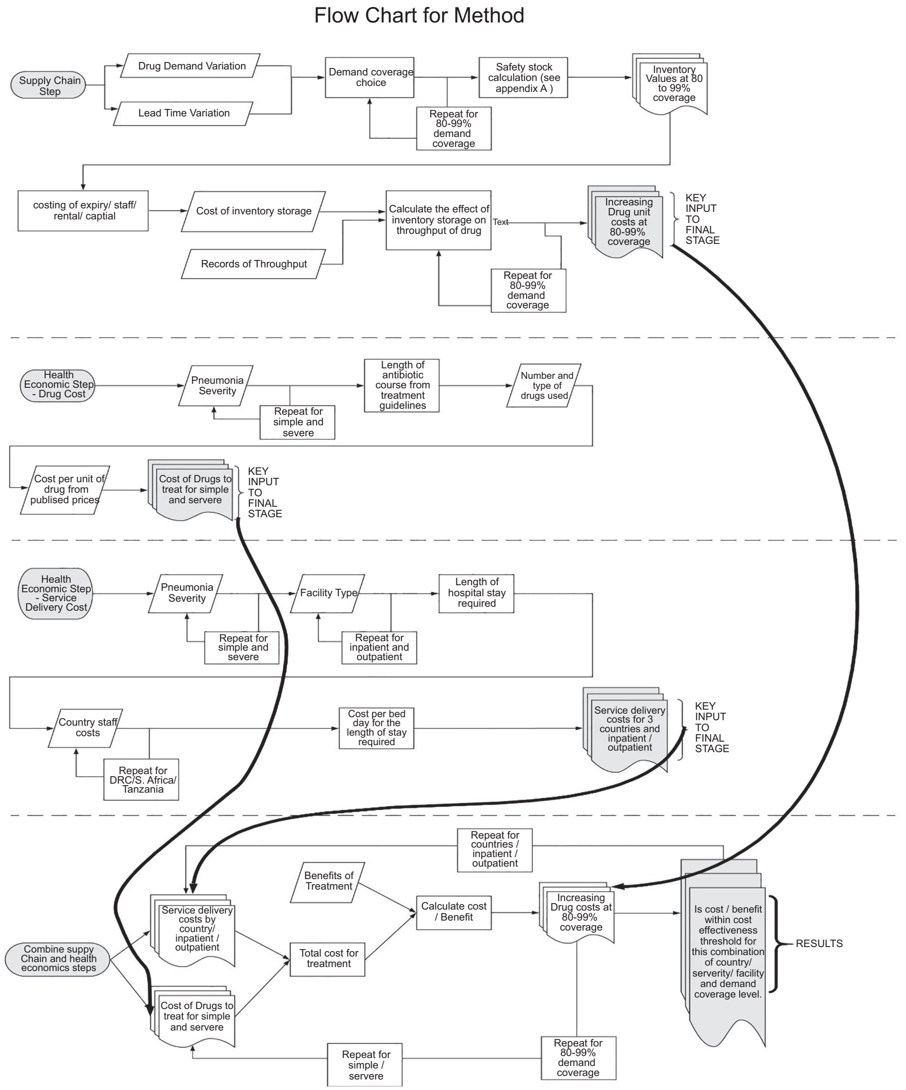

Figure 1.
Flowchart of Methodology

3.2 Storage costs

Storage costs are calculated as a percentage of the above inventory values. To calculate what that percentage requires data gathered from the four cost drivers; the first three were all available from the agency's accounts department and the last is a variable cost.

3.2.1 Driver 1: the space rented. The warehouse was rented at cost of 2m USD per year. It contained on average about 55m USD of drugs. That means the rental costs amount to 3.64 % of the cost of the inventory value.

3.2.2 Driver 2: the people needed to manage the inventory. The staff costs were 3m USD per year or 5.45% of the cost of the inventory value.

3.2.3 Driver 3: the expiries incurred. The rate of expiries was less than 2% of inventory value for each of the last five years.

3.2.4 Driver 4: the lost opportunity for interest in the bank. Interest rates at the time of writing were 1.15%.

Combining the four drivers results in a total storage cost at the time of writing of 12.23% of inventory value.

Sensitivity analysis covering a range of between 10 and 30% is detailed below to evaluate the influence of interest rates and agency-specific storage costs. At the time of writing, interest rates were very low and were only likely to increase in future. Also, since storage costs are specific to each aid agency, storage costs must be included in the sensitivity analysis in order to have generalizable findings that any aid agency might find useful.

The results below assume a storage cost of 25%, which would allow for significant interest rate rises and a considerable variation in organization-specific storage costs. These storage costs are presumed to be a simple linear relationship with inventory value increases.

3.3 Throughput

The throughput is simply the value of drugs dispatched to emergencies by the warehouse.

3.4 Effect on drug cost

The objective of this sensitivity analysis is to find the effect of various factors on drug cost. The easiest way to show the combination of the concepts is with an example supposing 90% demand coverage. Based on the supply chain equations, covering 90% of demand requires 5m USD of inventory value, and if annualized storage costs are 25%, then this equates to $\frac{25}{100} * 5\text{m}$ or 1.25m USD per year. If throughput were 15m USD of drugs dispatched, then the 1.25m storage cost would be adding $\frac{1.25}{15\,\text{million}} * 100$ or 8.33% to each packet of drugs served. Thus, at 90% coverage of emergency demand the drugs are 8.33% more expensive (meaning, 8.33% more expensive than if no inventory were stored). This same calculation is performed for each drug and each percentage of demand coverage. The percentage added depends on the underlying demand and lead time patterns, as well as the throughput compared to inventory value – these factors vary between drugs. The full tabulation is shown in Appendix 1.

3.5 Treatment costs

The baseline cost was in-country pneumonia treatment. That is, the cost to the country's ministry of health before adding the costs of aid agency drug storage. All costs are presented in US dollars as of 2014. It is worth remembering, there is no universal baseline as the cost of treating pneumonia varies, largely because there are different severities of pneumonia cases that might need more and different drugs and possibly inpatient care; where inpatient care is needed, the cost varies (e.g. because hospital staff salaries differ between countries).

So, a range of treatment costs at baseline was used, considering separately three different countries, two pneumonia severities and two facility types. The three countries were Democratic Republic of Congo (abbreviated DRC), Tanzania and South Africa, all of which are major recipients of aid from the agency studied and have a variety of income levels. Pneumonia severities were broken into nonsevere or severe, and facilities were classified as either clinic or primary hospital. However, all severe cases are treated at a primary hospital, so this creates three combinations for each country – nine total combinations – of baseline treatment costs from a wide range of circumstances to consider in the analysis.

There were four inputs needed to estimate the cost of treating the disease in each of the 9 baselines.

3.5.1 Input 1: the number of drugs used for each pneumonia severity. The standard treatment protocol recommended by WHO, 2014 was used to calculate the number of drugs needed. This gives the type and recommended daily doses of antibiotics for each severity of pneumonia, while the number of drugs is based on patient weight. Following the previously published method in Zhang *et al.* (2017), the average one-year-old child is assumed to weigh 10 kg.

3.5.2 Input 2: the cost of all the drugs that were used in treatment. All the prices for the drugs from input 1 were obtained, taken from the international drug price indicator guide (MSH, 2015), which is a document produced every few years to provide market research into the drug prices offered by suppliers and paid by ministries of health (MOH). The median supplier price was used (as opposed to the price paid by each MOH) because these supplier prices are available to all countries and agencies. The alternative would have been using the prices paid by each MOH in each specific country, however this would have introduced the problem that some countries, and thus the aid agency, might be willing to pay more for specific pack sizes (e.g. blister packs of 10 rather than bottles of one thousand tablets) which would introduce a choice other than inventory levels. While this may be an interesting avenue for future research, it distracts from the main intention of this study, which is the inventory-level decision. So, the supplier-side price available to all was preferred.

3.5.3 Input 3: service delivery time. The treatment duration was also taken from the WHO standard treatment protocol. It defined whether the care for each severity would be outpatient or inpatient and if the latter, how many bed days they would require.

3.5.4 Input 4: the service delivery costs. All the service delivery prices for input 3 were obtained, taken from the health economics department at WHO. They estimate costs of healthcare in their WHO-CHOICE initiative (WHO, 2011), which provides country-specific costs for outpatient visits and inpatient bed days. (e.g. health worker time, electricity, building maintenance)

3.6 Worked example of cost inputs

Taking all four inputs from above, consider the example of nonsevere cases of pneumonia treated at primary level hospitals in the DRC (i.e. DRC as the country, nonsevere pneumonia as the severity, primary level hospital as the facility level). First, the WHO recommends administering oral amoxicillin – 40 mg/kg twice daily for five days – to patients with nonsevere pneumonia. For a 10 kg infant, this gives a total of $40 \times 10 \times 5$ or 4,000 mg oral Aaoxicillin. Considering the price from the international drug price indicator guide for amoxicillin (0.0000736 USD per mg), the drug costs for simple pneumonia are $4{,}000 \times 0.0000736$ USD or 0.29 USD per episode. In addition to the cost of the drugs themselves, the WHO guidelines recommend outpatient treatment for nonsevere pneumonia. The outpatient treatment costs for a primary level hospital in DRC are estimated by WHO-CHOICE to be 0.57 USD. Adding the cost of drugs with the costs of service delivery, the estimated total cost for an average one-year-old with simple pneumonia at a primary hospital in DRC, using outpatient care, is 0.86 USD. Table 1 summarizes these calculations.

Table 1.
Worked example of baseline costing

Congo, dem. Rep./ Non-Severe pneumonia / primary hospital level	Units required to treat one episode	Cost per unit (USD)	Total cost (USD)
Oral amoxicillin	4,000 mg	0.0000736	0.29
Outpatient visit	1 visit	0.57	0.57
Total cost to treat			0.86

This method allows the separation of the drug costs from the total treatment costs so that later the storage costs can be added only to the drug component. The complete matrix for all combinations of countries, severities and facilities levels is shown in Appendix 3.

3.7 Cost-effectiveness

Once the baseline cost was established, then the benefits were found. The costs were measured in USD, while the benefits are measured in health outcomes, expressed in disability adjusted life years (DALYS) averted. The DALY can be thought of as one lost year of healthy life. Lost years of healthy life are averted by providing pneumonia treatment.

3.8 Cost-effectiveness

Just as the method costed a single episode of pneumonia, the interest is in DALYs averted by treating a single case of pneumonia. This paper follows the methods of the disease control priorities project (Simoes *et al.*, 2006) which takes into account the reduction in the chance of fatality and of those who lived, the reduction in disease duration. Following the published method, from sub-Saharan Africa, treating one case averted 0.083 DALYs for nonsevere and 0.043 DALYs for severe pneumonia. As with the published method the DALY benefits are assumed to be the same across all countries in the region.

3.9 Cost-effectiveness thresholds

Treatment costs go up as the storage cost at the aid agency, for increasing demand coverage adds an increasing percentage to the drug costs. But DALY benefits of treating one episode of pneumonia remain the same. So the cost-effectiveness ratio worsens.

The point is to see how much worse, particularly comparing it to established thresholds for good value. The cost-effectiveness thresholds in this paper are taken from the WHO's Commission on Macroeconomics and Health (WHO, 2001); this takes into account that what is considered good value in a high-income country might not be in a low-income country. They use thresholds for good value that vary according to a country's income.

An intervention that, per DALY averted, costs less than three times the national annual gross domestic product (GDP) per capita of the country is considered cost-effective, whereas one that costs less than once the national annual GDP per capita is considered highly cost-effective. These thresholds can be calculated for the countries used in this paper. This was done according to the World Bank figures for 2014 (World Bank, 2019). Based on GDP per capita, to be highly cost-effective when adding in increasing aid agency storage costs, DRC needs to be below 397 USD per DALY averted, Tanzania needs to be below 806 USD per DALY averted and South Africa needs to be below 7,582 USD per DALY averted.

4. Sensitivity analysis

4.1 Results for effect on drug cost

Figures 2–4 show the first part of the results, the costs of increasing demand coverage on drug costs. Plotted against each percentage increase in demand coverage is the required increase in inventory value in USD and storage cost in USD (at 25% storage cost) and on the secondary axis, the % added to drug cost.

It is evident that the graphs are not linear – the relationship between USD inventory and demand coverage is exponential. So, moving the one percent from 98 to 99% costs far more than from 80 to 81% because high demand coverage involves covering two things: busy periods and late supplier deliveries. The highest extremes of each are rare but also independent of one another, so the coincidence of the highest of all demand happening at the same time with the longest of all delays is extremely rare. The result is that to cover worst

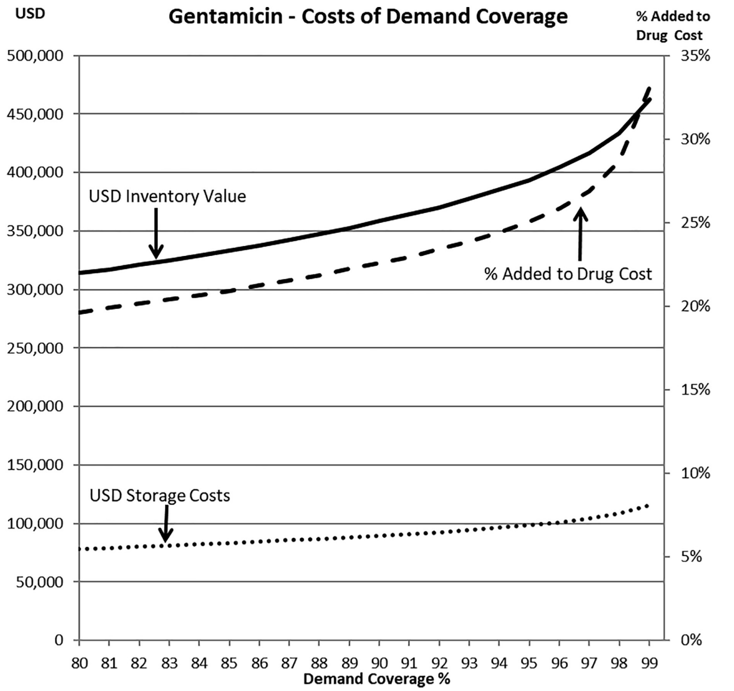

Figure 2.
The costs of increasing demand coverage for gentamicin

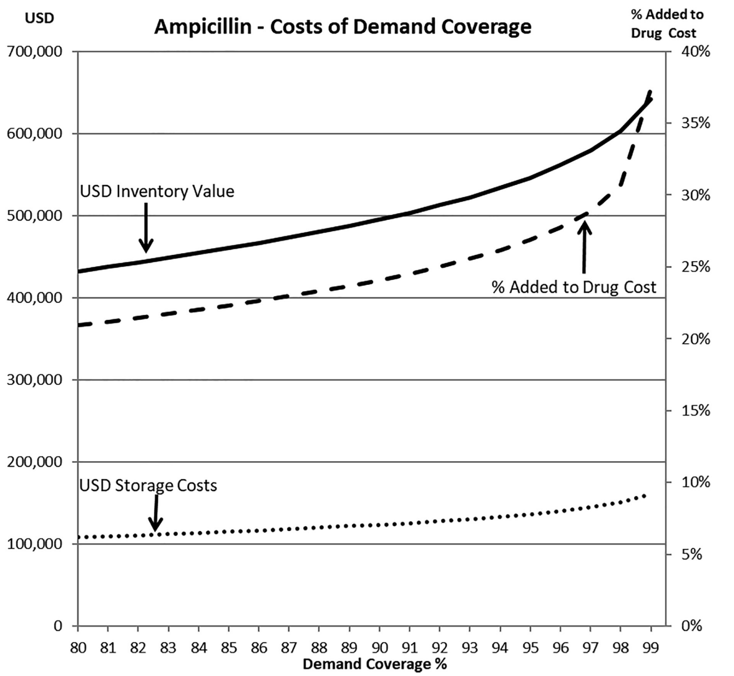

Figure 3.
The costs of increasing demand coverage for ampicillin

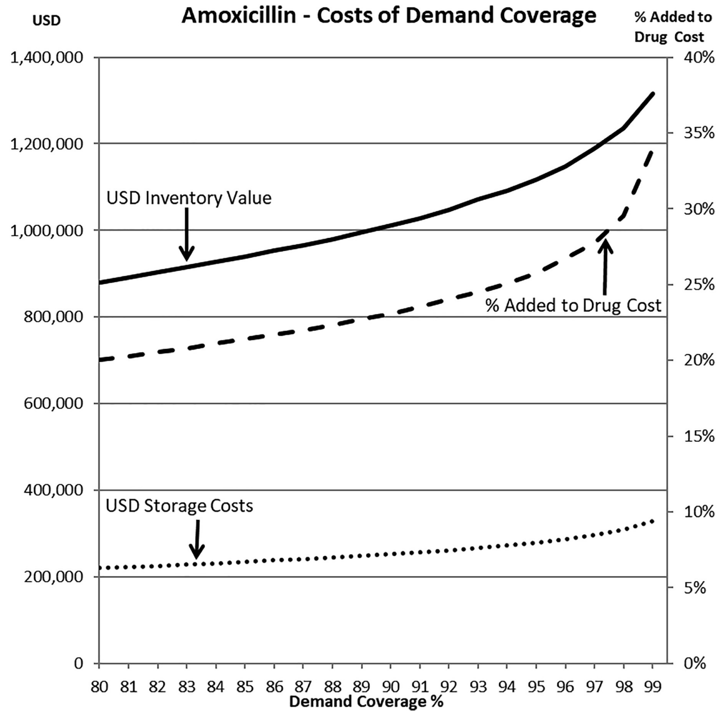

Figure 4.
The costs of increasing demand coverage for amoxicillin

case scenarios, and thus cover into the high 90s, each extra percentage requires rapidly ascending inventory value.

However, storage costs are only a percentage of inventory value. The following analysis focuses on 25%. Once these storage costs are known, they were added to the throughput to show the effect on the cost of a packet of drugs. For example, it can be seen that for amoxicillin at 80% demand coverage the drugs are 20% more expensive (compared to if no inventory had been stored), and at 99% demand coverage this goes up to 33% more expensive per packet.

The next part is to see the effect of this drug cost increase on total treatment cost and how this compares to good value. This is shown below for each of the nine different baselines in turn. It is expressed as the worsening CER and what the worse CER becomes as a percentage of good value threshold (HCET).

4.1.1 DRC, nonsevere, health facility level. The baseline CER to the MOH is 9.57 USD per DALY, compared to HCET in DRC of 398 USD per DALY. That is, at baseline, CER = 9.57 / 398 or CER = 2.41% of HCET. Addition of aid agency storage is shown in Figure 5. At 80% demand coverage, costs increase to 10.27 USD per DALY or CER = 2.58% of HCET. At 99% demand coverage, the costs increase to 10.78 USD per DALY or CER = 2.71% of HCET.

4.1.2 DRC, nonsevere, primary hospital level. The baseline CER to the MOH is 10.41 USD per DALY, compared to HCET in DRC of 398 USD per DALY. That is, at baseline, CER = 10.41 / 398 or CER = 2.62% of HCET. Addition of aid agency storage costs is shown in Figure 6. At 80% demand coverage, costs increase to 11.12 USD per DALY or CER = 2.80% of HCET. At 99% demand coverage, the costs increase to 11.62 USD per DALY or CER = 2.92% of HCET.

4.1.3 DRC, severe, primary hospital level. The baseline CER to the MOH is 180.34 USD per DALY, compared to HCET in DRC of 398 USD per DALY. That is, at baseline, CER = 180.34 /

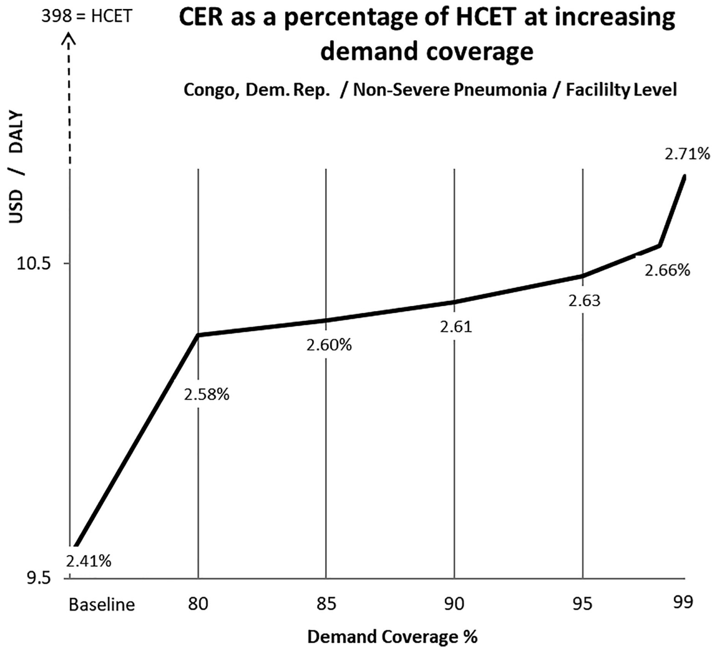

Figure 5.
DRC, nonsevere, health facility: Pneumonia treatment cost-effectiveness as a percentage of HCET at increasing demand coverage

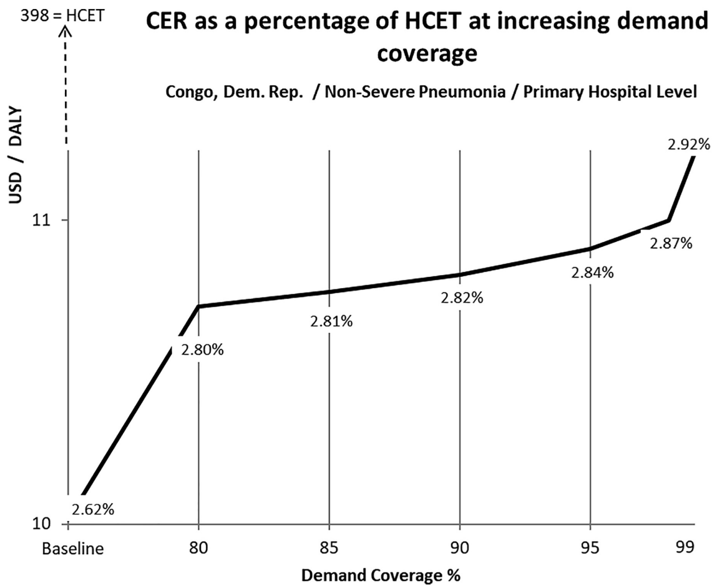

Figure 6.
DRC, nonsevere, primary hospital: Pneumonia treatment cost-effectiveness as a percentage of HCET at increasing demand coverage

398 or CER = 45.36% of HCET. Addition of aid agency storage costs is shown in Figure 7. At 80% demand coverage, costs increase to 198.25 USD per DALY or CER = 48.87% of HCET. At 99% demand coverage, the costs increase to 206.91 USD per DALY or CER = 52.04% of HCET.

4.1.4 Tanzania, nonsevere, facility level. The baseline CER to the MOH is 16.92 USD per DALY, compared to HCET in Tanzania of 806.15 USD per DALY. That is, at baseline, CER = 16.92/806.15 or 2.10% of HCET. Addition of aid agency storage costs is shown in Figure 9. At 80% demand coverage, costs increase to 17.62 USD per DALY or CER = 2.19% of HCET. At 99% demand coverage the costs increase to 18.13 USD per DALY or CER = 2.25% of HCET.

4.1.5 Tanzania, nonsevere, primary hospital level. The baseline CER to the MOH is 18.85 USD per DALY, compared to HCET in Tanzania of 806.15 USD per DALY. That is, at baseline, CER = 18.85 / 806.15 or 2.34% of HCET. Addition of aid agency storage costs is shown in Figure 8. At 80% demand coverage, costs increase to 19.55 USD per DALY or CER = 2.43% of HCET. At 99% demand coverage the costs increase to 20.05 USD per DALY or CER = 2.49% of HCET.

4.1.6 Tanzania, severe, primary hospital level. The baseline CER to the MOH is 450.83 USD per DALY, compared to HCET in Tanzania of 806.15 USD per DALY. That is, at baseline, CER = 450.83 / 806.15 or 55.92% of HCET. Addition of aid agency storage costs is shown in Figure 11. At 80% demand coverage, costs increase to 465.75 USD per DALY or CER = 57.78% of HCET. At 99% demand coverage the costs increase to 477.53 USD per DALY or CER = 59.24% of HCET.

4.1.7 South Africa, nonsevere, facility level. The baseline CER to the MOH is 118.49 USD per DALY, compared to HCET in South Africa of 7,582 USD per DALY. That is, at baseline, CER = 118.49 / 7,582 or 1.56% of HCET. Addition of aid agency storage costs is shown in

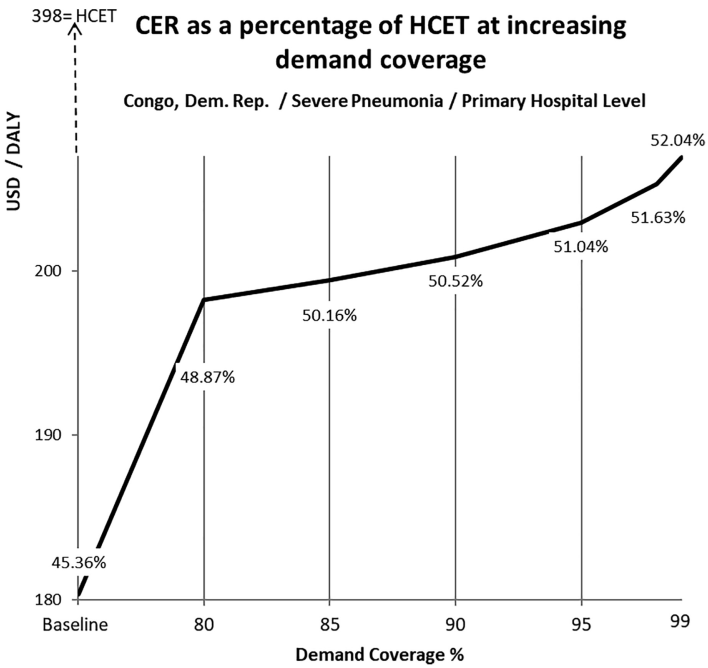

Figure 7.
DRC, severe, primary hospital: Pneumonia treatment cost-effectiveness as a percentage of HCET at increasing demand coverage

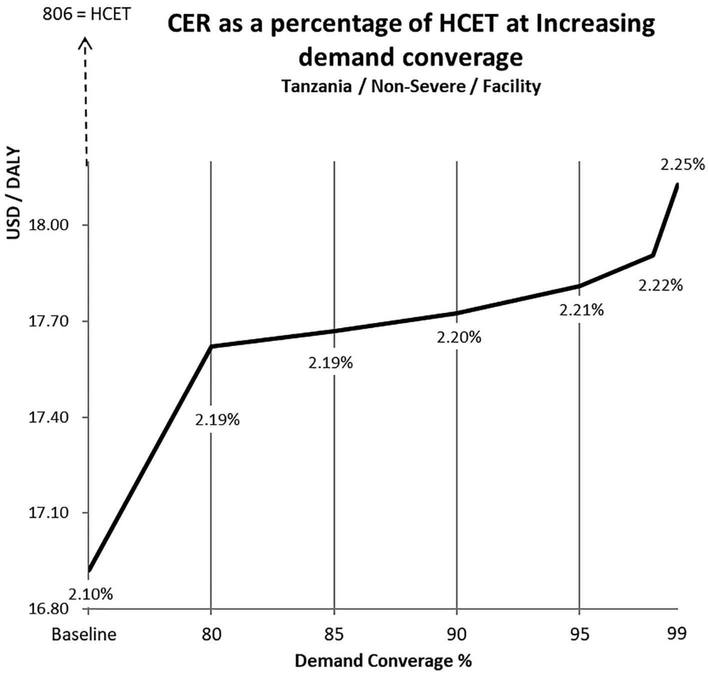

Figure 8.
Tanzania, nonsevere, primary hospital: Pneumonia treatment cost- effectiveness as a percentage of HCET at increasing demand coverage

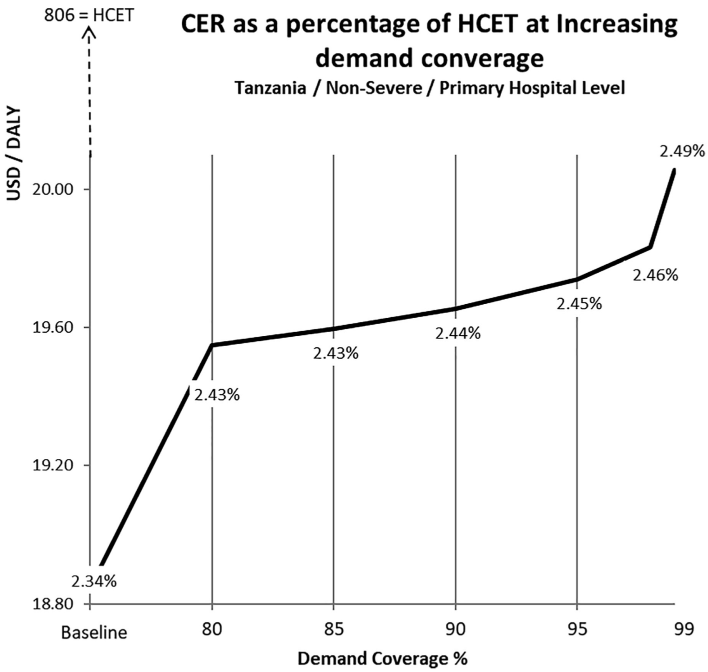

Figure 9.
Tanzania, nonsevere, health facility: Pneumonia treatment cost- effectiveness as a percentage of HCET at increasing demand coverage

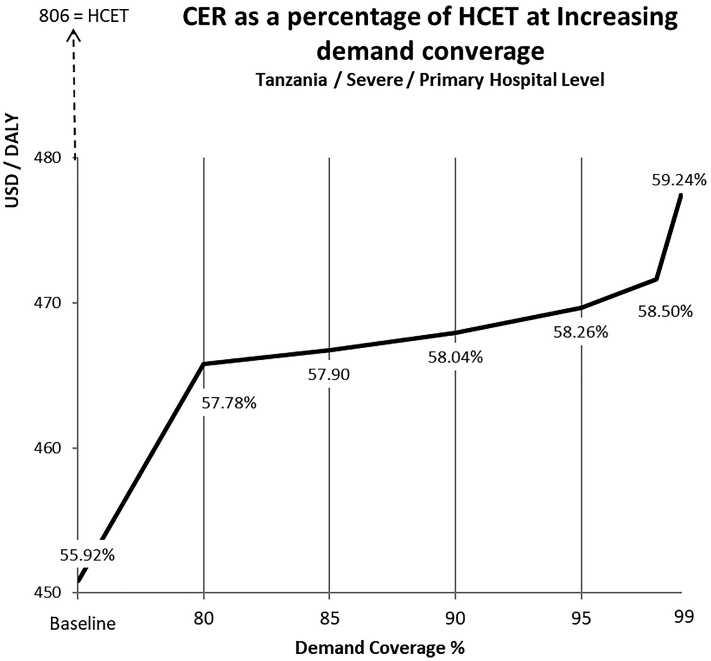

Figure 10. Tanzania, severe, primary hospital: Pneumonia treatment cost effectiveness as a percentage of HCET at increasing demand coverage

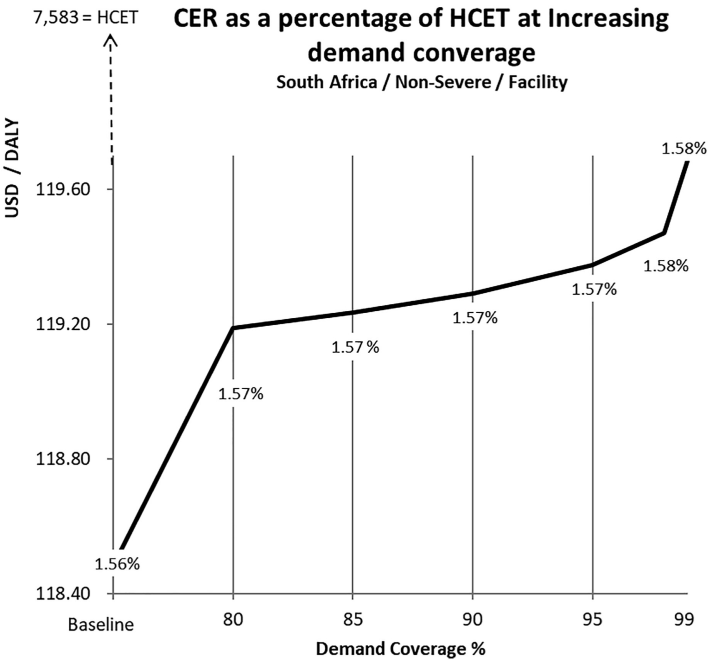

Figure 11. South Africa, nonsevere, health facility: Pneumonia treatment cost-effectiveness as a percentage of HCET at increasing demand coverage

Figure 10. At 80% demand coverage, costs increase to 119.19 USD per DALY or CER = 1.57% of HCET. At 99% demand coverage the costs increase to 119.69 USD per DALY or CER = 1.58% of HCET.

4.1.8 South Africa, nonsevere, primary hospital level. The baseline CER to the MOH is 134.51 USD per DALY, compared to HCET in South Africa of 7,582 USD per DALY. That is, at baseline, CER = 134.51 / 7,582 or 1.77% of HCET. Addition of aid agency storage costs is shown in Figure 12. At 80% demand coverage, costs increase to 135.21 USD per DALY or CER = 1.78% of HCET. At 99% demand coverage the costs increase to 135.71 USD per DALY or CER = 1.79% of HCET.

4.1.9 South Africa, severe, primary hospital level. The baseline CER to the MOH is 6498.51 USD per DALY, compared to HCET in South Africa of 7,582 USD per DALY. That is, at baseline, CER = 6498.51 / 7,582 or 85.70% of HCET. Addition of aid agency storage costs is shown in Figure 13. At 80% demand coverage, costs increase to 6513.43 USD per DALY or CER = 85.90% of HCET. At 99% demand coverage the costs increase to 6525.21 USD per DALY or CER = 86.06% of HCET.

5. Results

The results show the aid agency could increase from 80% all the way to 99% demand coverage. The pneumonia treatment remains highly cost effective. This is true for all the combinations of country, pneumonia severity and facility type. Moreover, the strictest criterion of high cost-effectiveness was used. This is the most stringent criteria and demands the treatment cost to be three times lower than the threshold for cost-effectiveness (WHO, 2001). Furthermore, the main analysis was done using sensitivity of 25% storage cost, an upper end costing of storage. In conclusion, increasing to 99% is robustly shown to be highly cost effective.

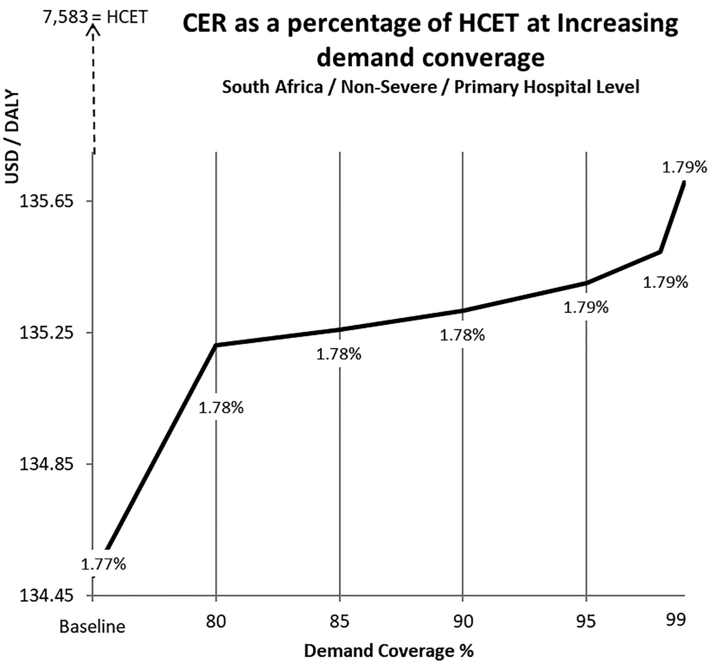

Figure 12.
South Africa, non-severe, primary hospital: Pneumonia treatment cost effectiveness as a percentage of HCET at increasing demand coverage

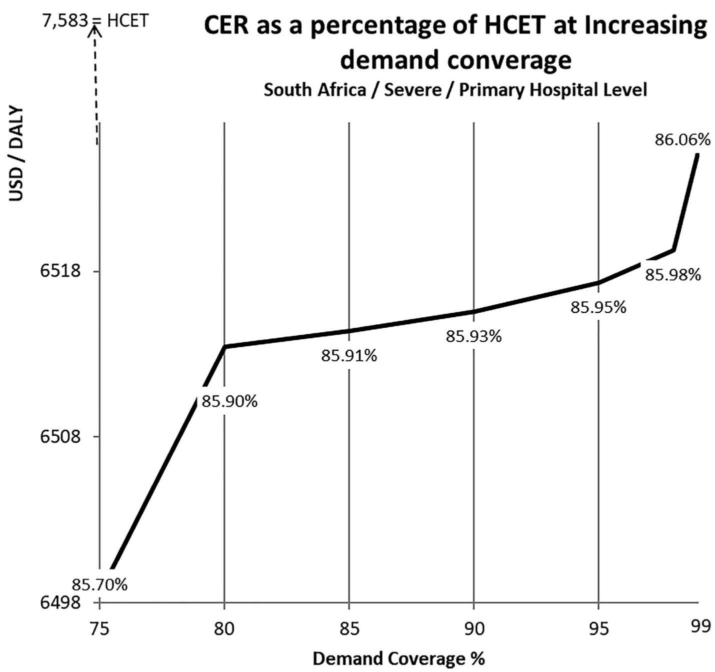

Figure 13.
South Africa, severe, primary hospital: Pneumonia treatment cost effectiveness as a percentage of HCET at increasing demand coverage

While all combinations of country and severity are highly cost-effective there are specific features. First, treatment of nonsevere pneumonia is the most cost-effective at baseline (cost to MOH), and even increasing aid agency storage costs to 99% demand coverage adds less than 1% to the CER as % of HCET. Meaning for nonsevere, even with drugs stored at 99% demand coverage, the CER as % of HCET remains below 3%, in all facilities and countries. Second, higher income countries show smaller increases in treatment cost when increasing demand coverage. This is because the drug component of treatment is relatively small compared to service delivery (particularly staff) costs. So for South Africa, nonsevere, facility level, moving from current 80%–99% incurs only a 0.01% increase in CER as a percentage of HCET, whereas for DRC it is 0.51%. Third, treatment of severe pneumonia comes the closest to threatening to fall below the threshold of highly cost-effective because the baseline is higher. Take South Africa as an example, the baseline level starts at 85.7% of the HCET. That being said, the dominance in staff costs there means that even at 99% drug storage costs are only adding 0.36% of HCET. The largest percentage increase in CER as a % HCET comes from severe pneumonia in the lowest income setting, in DRC, where an increase of 6.68% takes place – but the relatively low baseline of 45.36% means even at 99% only reaching 52.04 % CER as a % HCET. So, over all combinations, even the greatest increase is still only 6.68% percent increase in CER as a % HCET and only reaches 52.04% CER/HCET.

Finally, the increases of CER as a % HCET are small. Good value is maintained across the board as the costs are increasing by only fractions of fractions; that is to say, the storage costs are a fraction of the inventory value of the drugs, the storage costs are an even smaller fraction of the throughput and the drugs themselves are a fraction of treatment costs. And for such a highly cost-effective treatment, the starting CER is only a fraction of the HCET, thus multiplying fractions of fractions of fractions. Even the steep rises in the amount of inventory value for upper percentages of demand coverage are very diluted by the time they are applied to CER as a % HCET.

This translates, on the ground, to the aid agency dealing with acute drug shortages, where there is no need to pay for already existing infrastructure and staffs since these are already in place (more on this assumption below). The cost of providing extra treatments in crisis is limited to providing drugs. Further, for any treatment, the drugs would have had to be provided by the MOH anyway so only adding in the storage cost of drugs.

The direction of findings is not unexpected. One question that might arise is why the agency have only held at 80%. This means missing 20% of demand. It might seem obvious that storage costs will not add that much to treatment costs, however the extent to which the treatments remain highly cost effective is a surprising finding and not possible without fully cost modeling. No health economic studies had been done at the agency. More generally, to the best of the authors' knowledge, there are no examples of published research which combine health economics and inventory control. One major reason why demand coverage might be low is a lack of health economic method in operational decision-making.

Another reason is that the method used here is not simple to repeat. The way it is presented as a step-by-step process might give the impression of being straightforward. However, even the first step, establishing that current demand coverage is 80%, requires well-run supply chain systems. Many less well-resourced operations/agencies would not measure demand coverage, so even the first step of the method could not be completed.

Furthermore, without decision support to give economic guidance, a possible objection to increasing inventory is perceived inefficiency. At the agency in question, audits compared aid inventory to established norms in the commercial sector. These tend to make humanitarian operations look bad. Emergency demand is erratic and so, to provide good demand coverage, the inventory levels have to be very high. Sometimes up to many multiples of equivalent demand coverage from commercial warehouses. This expense can hide the good value. It is only by looking beyond commercial comparisons and establishing a new method for the humanitarian sector that a better understanding of cost/benefit can be reached.

Another possible reason is that senior decision makers are normally from health rather than supply chain backgrounds. So for example, while looking at cost/benefit for a new medical treatment might be natural, it would not be intuitive to do the same for supply chains. As emphasized here, inventory decisions are yet to be looked at in heath economic terms. Suggestions of increases in inventory might be more appealing to public health professionals once their worth is presented in the vocabulary of the health sector, especially when it can be shown that increased inventory is highly cost-effective. It may be that improvements in the supply chain are amongst the most highly cost-effective interventions in public health – but yet to be described in such terms.

6. Limitations

This paper is a first attempt at health economics in humanitarian inventory. There are several areas for further investigation.

For this agency, the method is valid for the majority of humanitarian response, but one limitation stands out. This method only applies where shortages of treatment can be addressed with additional drug supply alone. Sometimes drug supply is not enough. For example, in conflicts, the flight of local medical staff might mean aid agency physicians are required to directly administer treatments. The salaries across agencies will be different and likely different again from the in-country ministry of health. That said, for the agency, of the hundreds of millions of dollars of drugs sent to crises each year, most was administered through existing ministry of health staff, only a tiny fraction was accompanied teams of physicians to directly administer treatments.

There is also a counterpoint to this limitation. In the assumptions of this method, facilities and staff exist but there are shortages of drugs. Under these circumstances, it could be argued that the additional cost of providing treatment should not include service delivery costs at all. This is because the staff and infrastructure are present and paid for anyway and simply going to waste in the absence of drugs. The complexity of what staff costs amount to would require time on the ground. In particular, swapping the perspective of an agency warehouse for that of the country receiving the drugs. This paper limits itself to the view of drugs supplied adding to already existing in country costs – the main type of intervention.

Another limitation is lack of comparisons. While increased inventory is cost-effective, something else might be more cost-effective. There is wide scope to perform comparisons in future. This could include comparing the option of higher inventory investment in an existing treatment program to, for example, the introduction of a completely new health program. However for now, even without comparisons, the retention of highly cost-effective treatments even at the highest inventory levels strongly suggest it should be on the table as a possible choice. In future, comparisons would add to the usefulness.

From other published work, it can be seen that working out the baseline CER is subject to methodological variations (Zhang *et al.*, 2016). The baseline used here was in line with several published studies, but the area is controversial.

Only one disease treatment was looked at. Other treatments might behave quite differently, particularly depending on the percentage of the total treatment cost which was drug cost. Other differences would come from the demand and lead-time patterns. It would be informative to work through all the different diseases treatments held at the warehouse.

Last but not least is the big untapped possibility for future work. There is potential to expand the applicability enormously. Similar decisions but on a much larger scale are made by ministries of health in low-income countries. They have huge inventories to supply to hospitals nationwide. For example, in Kenya, the average inventory value in their main warehouses amounts to 125.4m USD (KEMSA, 2018). Extrapolated across low income countries, medical warehouses will hold billions of USD. They too have to decide on their inventory investment. Similar to aid agencies there is constrained funding and much competition for resource. There is potential application for health economics in ministry of health inventory-level decisions. There is huge USD value behind such unmet research questions.

Note

1. This concept may be best explained through an example: suppose that the current inventory level is enough to meet demand most of the year, resulting in five stockouts a year. Perhaps storing ten additional packets of drugs would reduce stockouts to three per year, while increasing the stock level by 20 would reduce annual stockouts to two. In this case, the first ten units of drugs are used twice per year, but the second group is only used once despite the fact that each unit costs the same to store

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Corresponding author
Robert A. Cook can be contacted at: racook2@neiu.edu

Appendix 1
Inventory costs at different demand coverage levels

The formula itself is written as below:

$$\text{Inventory Level} = z \times \sqrt{\mathbb{E}(L)\sigma_D^2 + \mathbb{E}(D)^2\sigma_L^2}$$

where

$z =$ The percentage of demand that to be covered

$\mathbb{E}(L) =$ The average lead time for the drugs

$\sigma_L =$ The variation of lead time for the drugs

$\mathbb{E}(D) =$ The average demand for the drugs

$\sigma_D =$ The variation of demand for the drugs

The formula was recalculated to give the inventory level needed with increasing amounts of demand covered (values for z), starting from the current 80% real world demand coverage and increasing up to 99.9%.

Appendix 2

Table A1. Tabulation of inventory values and storage costs with increasing demand coverage

Demand coverage	USD inventory value	Storage costs at 25%	Percentage added to drug costs
	Amoxicillin		
80%	880,259	220,065	10%
81%	892,184	223,046	10%
82%	902,784	225,696	11%
83%	914,709	228,677	11%
84%	926,634	231,659	11%
85%	939,884	234,971	11%
86%	953,134	238,284	12%
87%	966,384	241,596	12%
88%	979,634	244,909	12%
89%	995,534	248,884	13%
90%	1,011,434	252,859	13%
91%	1,028,659	257,165	13%
92%	1,047,209	261,802	14%
93%	1,071,059	267,765	14%
94%	1,090,934	272,734	15%
95%	1,117,434	279,359	15%
96%	1,147,909	286,977	16%
97%	1,190,309	297,577	17%
98%	1,236,684	309,171	19%
99%	1,316,184	329,046	20%
99.9%	1,514,934	378,734	23%

Demand coverage	USD inventory value	Storage costs at 25%	Percentage added to drug costs
	Ampicillin		
80%	432,218	108,055	10%
81%	438,104	109,526	10%
82%	443,009	110,752	11%
83%	448,895	112,224	11%
84%	454,781	113,695	11%
85%	460,667	115,167	11%
86%	466,553	116,638	12%
87%	473,420	118,355	12%
88%	480,287	120,072	12%
89%	487,154	121,789	13%
90%	495,002	123,751	13%
91%	502,850	125,713	13%
92%	512,660	128,165	14%
93%	522,470	130,618	14%
94%	534,242	133,561	15%

Demand coverage	USD inventory value	Storage costs at 25%	Percentage added to drug costs
	Ampicillin, cont.		
95%	546,014	136,504	15%
96%	561,710	140,428	16%

(*continued*)

Ampicillin, cont.			
Demand coverage	USD inventory value	Storage costs at 25%	Percentage added to drug costs
97%	579,368	144,842	17%
98%	602,912	150,728	19%
99%	642,152	160,538	20%
99.9%	781,454	195,364	23%

Gentamicin			
Demand coverage	USD inventory value	Storage costs at 25%	Percentage added to drug costs
80%	314,332	78,583	10%
81%	316,837	79,209	10%
82%	321,012	80,253	10%
83%	325,187	81,297	10%
84%	329,362	82,340	10%
85%	333,537	83,384	10%
86%	337,712	84,428	10%
87%	342,722	85,680	10%
88%	347,732	86,933	10%
89%	352,742	88,185	10%
90%	358,587	89,647	10%
91%	364,432	91,108	10%
92%	370,277	92,569	10%
93%	377,792	94,448	10%
94%	385,307	96,327	10%
95%	393,657	98,414	10%
96%	404,512	101,128	10%
97%	417,037	104,259	11%
98%	433,737	108,434	11%
99%	462,962	115,740	11%
99.9%	534,772	133,693	11%

Table A1.

Appendix 3

Table A2. Tabulation of Baseline CER and Increasing Costs with Higher Demand Coverage

Country Pneumonia Severity Facility	Cost / Benefit element	Baseline–costs to MOH Quantity Required	USD cost per unit	USD/Utility per episode Treated	Costs with aid agency stored drugs at increasing demand coverage 80%	85%	90%	95%	98%	99%
Congo, Dem. rep.	Amoxicillin	4,000 mg	0.0000736	0.29	0.35	0.36	0.36	0.37	0.38	0.38
Nonsevere	Outpatient visit	1 visit	0.5	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Clinic level	Total cost to treat			0.79	0.85	0.86	0.86	0.87	0.88	0.88
	Utility in DALY			0.08	0.08	0.08	0.08	0.08	0.08	0.08
	CER in USD Per Daly			9.57	10.27	10.32	10.38	10.46	10.56	10.62
	% Increase USD per DALY				7.32	7.82	8.42	9.30	10.29	10.95
Congo, Dem. rep.	Amoxicillin	4,000 mg	0.0000736	0.29	0.35	0.36	0.36	0.37	0.38	0.38
Nonsevere	Outpatient Visit	1 visit	0.57	0.57	0.57	0.57	0.57	0.57	0.57	0.57
Primary hospital level	Total Cost to Treat			0.86	0.92	0.93	0.93	0.94	0.95	0.95
	Utility in DALY			0.08	0.08	0.08	0.08	0.08	0.08	0.08
	CER in USD Per Daly			10.41	11.12	11.16	11.22	11.30	11.40	11.46
	% Increase USD per DALY				6.73	7.19	7.73	8.55	9.46	10.07
Congo, Dem. Rep.	Ampicillin	15,000 mg	0.00017	2.55	3.08	3.11	3.15	3.22	3.29	3.33
Severe	Gentamicin	375 mg	0.0015625	0.59	0.70	0.71	0.72	0.73	0.74	0.75
Primary hospital level	Inpatient	5 days	0.9238	4.62	4.62	4.62	4.62	4.62	4.62	4.62
	Total Cost to Treat			7.75	8.40	8.44	8.49	8.56	8.65	8.71
	Utility in DALY			0.04	0.04	0.04	0.04	0.04	0.04	0.04
	CER in USD Per Daly			180.35	195.27	196.24	197.42	199.17	201.12	202.48
	% Increase USD per DALY				8.27	8.81	9.47	10.44	11.52	12.27

Country Pneumonia Severity Facility	Cost / Benefit element	Baseline–costs to MOH Quantity Required	USD cost per unit	USD/Utility per episode Treated	Costs with aid agency stored drugs at increasing demand coverage 80%	85%	90%	95%	98%	99%
Tanzania	Amoxicillin	4,000 mg	0.0000736	0.29	0.35	0.36	0.36	0.37	0.38	0.38
Nonsevere	Outpatient visit	1 visit	1.11	1.11	1.11	1.11	1.11	1.11	1.11	1.11
Facility level	Total cost to Treat			1.40	1.46	1.47	1.47	1.48	1.49	1.49
	Utility in DALY			0.08	0.08	0.08	0.08	0.08	0.08	0.08
	CER in USD per Daly			16.92	17.62	17.67	17.73	17.81	17.91	17.97
	% Increase USD per DALY				4.14	4.42	4.76	5.26	5.82	6.20

(*continued*)

Table A2.

Country / Pneumonia / Severity / Facility	Cost / Benefit element	Baseline–costs to MOH: Quantity Required	USD cost per unit	USD/Utility per episode Treated	Costs with aid agency stored drugs at increasing demand coverage: 80%	85%	90%	95%	98%	99%
Tanzania	Amoxicillin	4,000 mg	0.0000736	0.29	0.35	0.36	0.36	0.37	0.38	0.38
Nonsevere	Outpatient visit	1 visit	1.27	1.27	1.27	1.27	1.27	1.27	1.27	1.27
Primary hospital level	Total cost to treat			1.56	1.62	1.63	1.63	1.64	1.65	1.65
	Utility in DALY			0.08	0.08	0.08	0.08	0.08	0.08	0.08
	CER in USD per Daly			18.85	19.55	19.60	19.65	19.74	19.83	19.90
	% Increase USD per DALY				3.72	3.97	4.27	4.72	5.23	5.56
Tanzania	Ampicillin	15,000 mg	0.00017	2.55	3.08	3.11	3.15	3.22	3.29	3.33
Severe	Gentamicin	375 mg	0.0015625	0.59	0.70	0.71	0.72	0.73	0.74	0.75
Primary hospital level	Inpatient	5 days	3.25	16.25	16.25	16.25	16.25	16.25	16.25	16.25
	Total cost to treat			19.39	20.03	20.07	20.12	20.20	20.28	20.34
	Utility in DALY			0.04	0.04	0.04	0.04	0.04	0.04	0.04
	CER in USD Per Daly			450.84	465.76	466.73	467.91	469.66	471.61	472.97
	% Increase USD per DALY				3.31	3.52	3.79	4.17	4.61	4.91

Country / Pneumonia / Severity / Facility	Cost / Benefit element	Baseline–costs to MOH: Quantity Required	USD cost per unit	USD/Utility per episode Treated	Costs with aid agency stored drugs at increasing demand coverage: 80%	85%	90%	95%	98%	99%
South Africa	Amoxicillin	4,000 mg	0.0000736	0.29	0.35	0.36	0.36	0.37	0.38	0.38
Nonsevere	Outpatient Visit	1 visit	9.54	9.54	9.54	9.54	9.54	9.54	9.54	9.54
Facility level	Total Cost to Treat			9.83	9.89	9.90	9.90	9.91	9.92	9.92
	Utility in DALY			0.08	0.08	0.08	0.08	0.08	0.08	0.08
	CER in USD Per Daly			118.49	119.19	119.24	119.29	119.38	119.47	119.53
	% Increase USD per DALY				0.59	0.63	0.68	0.75	0.83	0.88
South Africa	Amoxicillin	4,000 mg	0.0000736	0.29	0.35	0.36	0.36	0.37	0.38	0.38
Nonsevere	Outpatient Visit	1 visit	10.87	10.87	10.87	10.87	10.87	10.87	10.87	10.87
Primary hospital level	Total Cost to Treat			11.16	11.22	11.23	11.23	11.24	11.25	11.25
	Utility			0.08	0.08	0.08	0.08	0.08	0.08	0.08
	CER in USD Per Daly			134.51	135.21	135.26	135.32	135.40	135.50	135.56
	% Increase USD per DALY				0.52	0.56	0.60	0.66	0.73	0.78
	Gentamicin	375	0.0015625	0.59	0.70	0.71	0.72	0.73	0.74	0.75
	Inpatient	5	55.26	276.30	276.30	276.30	276.30	276.30	276.30	276.30
	Total cost to treat			279.44	280.08	280.12	280.17	280.25	280.33	280.39
	Utility in DALY			0.04	0.04	0.04	0.04	0.04	0.04	0.04
	CER in USD Per Daly			6498.5	6513.4	6514.4	6515.6	6517.3	6519.3	6520.7
	% Increase USD per DALY				0.23	0.24	0.26	0.29	0.32	0.34