HOW ECONOMIC DEVELOPMENT
AFFECTS ANTIBIOTIC RESISTANCE

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Abstract

Initially, economic development increases resistance because migration of people to urban areas in developing countries increases incomes, crowding and the use of antibiotics. Also, developing countries often don't require prescriptions or distribute high quality antibiotics. In developed countries, antibiotic resistance often falls or there is a decline in the rate of growth of resistance because infections decline with improvements in water quality, sanitation, housing and nutrition. However, in developed countries most antibiotics are used to treat food animals rather than humans. The use of antibiotics to treat food animals creates a risk that the effectiveness of antibiotics to treat humans will be reduced. However, evidence seems to indicate that antibiotic use in animals has had little effect on antibiotic resistance in humans.

Key Words: economic development, antibiotic resistance, antimicrobial resistance

JEL Classification: D62, I15, I18, O15, R23

Introduction

> The consequences [of antibiotic resistance] are severe. Infections caused by resistant microbes fail to respond to treatment, resulting in prolonged illness and greater risk of death. Treatment failures also lead to longer periods of infectivity, which increase the numbers of infected people moving in the community and thus expose the general population to the risk of contracting a resistant strain of infection. (World Health Organization 2002).

This quotation illustrates the potential consequences of antibiotic resistance. Students are often interested in staying alive. Beyond the potential health consequences, antibiotic resistance is a useful way to teach how positive and negative externalities affect efficiency. Also, showing how economic development affects antibiotic resistance illustrates how the demand curve is affected by changes in income, the number of buyers, and insurance.

Externalities exist when either the benefits or costs of consumption or production spill over onto other people who did not agree to the action. Antimicrobial use creates both negative and positive externalities (Coast et al. 1998 and Horowitz and Moehring 2004). It creates a negative externality because antibiotics eliminate the less resistant bacteria while leaving the more resistant bacteria to multiply. These resistant microbes then infect others and reduce the

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effectiveness of antimicrobials to them. This implies that the marginal costs incurred from a treatment include both the marginal cost of the treatment (*MC*) itself and the marginal external cost (*MEC*) from the resistant microbes.

Antimicrobial use creates a positive externality by reducing the number of infected people who in turn are less likely to infect others, thereby improving public health. This implies that the marginal benefit of treatment includes both the marginal benefit of treatment (*MB*) and the marginal external benefit from improved public health (*MEB*).

Efficient anti-microbial use occurs when the marginal benefit of treatment equals the marginal costs incurred from the treatment to both the person being treated and to others. Excessive antibiotics are used because users don't bear the full cost of treatment in the future.

Previous articles have explored how the negative externality from antibiotic resistance can be reduced by prevention and improved diagnosis (World Bank 1993), substitutes (Howard 2004), property rights (Horowitz and Moehring 2004), taxation (Coast et al. 1998), regulation (Coast et al. 1998), tradeable permits (Coast et al. 1998), surveillance (Horan et al. 2008) and treaties (Anomaly 2010). These articles, however, do not explore the effect of economic development on antibiotic resistance.

Economic development has two contradictory effects on microbial resistance to antibiotics: First, economic development may increase resistance, since more people can afford antibiotics. A key determinate in antibiotic resistance is the volume of antibiotic exposure (Austin et al. 1999) such that countries that use more antibiotics tend to have more resistant bacteria (Bronzwaer et al., 2002 and Costelloe et al., 2010). Second, economic development may reduce microbial resistance to antibiotics since countries can afford more effective infection control and better public health. The reduction in disease reduces antibiotic use in humans and potentially microbial resistance. As countries develop, however, antibiotic resistance may increase as more antibiotics are used on animals. Hence, the effect of economic development on microbial resistance is ambiguous.

Silbergeld et al. (2008) argue that there are four reasons why antibiotic use in agricultural is a major cause for concern. First, the largest use of antibiotics in the world is in agriculture. Second, much of the use of antibiotics in agriculture is sub-therapeutic exposure to antibiotics. Third, every important class of antibiotic is used in agriculture. And fourth, humans are exposed to resistant bacteria through consuming animal products and through release into the environment.

However, reducing or restricting antibiotic use in agriculture may actually increase antibiotic resistance. This is because healthier animals are less likely to pass on resistant bacteria to humans. Singer et al. (2007) list three reasons why diseased animals increase foodborne pathogen levels. First, diseased animals are more likely to spread pathogens. Second, diseased parts of diseased animals must be removed in processing plants which increases the risk of contamination and cross contamination. Third, diseased animals increase the risk that processing plant mistakes such as gastrointestinal ruptures will contaminate the meat from that animal and other animals. They conclude that small improvements in animal health may result in large improvements in human health. Likewise, Hurd et al. (2008) conclude that small improvements in animal health greatly reduce the risk of human sickness from foodborne illnesses.

Alban et al. (2008), Hurd et al. (2008) and Hurd et al. (2004) conclude that reducing antibiotic use in animals leads to higher risk from illness from animals while the human risks

from antibiotic resistance from animals is very low. Cox et al. (2009) find that current penicillin use in food animals in the United States creates almost zero human health risks and Cox et al. (2004) find that a ban on Virginiamycin (VM) would have almost no benefit for human health. Cox et al. (2006) find that stopping animal antibiotic use would probably cause much more human illness than it would prevent.

This article examines how economic development affects microbial resistance to antibiotics. Because many antimicrobials are used in animal husbandry, developed countries may use more antibiotics than developing countries. However, human antibiotic use is likely to decline as the levels of human sickness decline. For simplicity, the analysis below assumes buyers purchase antibiotics solely for human use.

How economic development affects the demand for antibiotics and efficiency

Suppose that the demand curve for a representative buyer is $P_i = a_i - bq_i$ where q_i measures the quantity of antibiotic treatments used by each buyer in country i, b is the slope of the demand curve, P_i is the price of an antibiotic treatment in country i, and a_i is the maximum price that a buyer will spend on a antibiotic treatment in country i.

The buyer's income and the price of substitutes determine a_i. An increase in income or an increase in the price of a substitute will cause a parallel shift to the right in the demand curve.

Since government and private insurance programs pay much of the cost of many antibiotics, let s_i be the portion of the price paid by the buyer in country i (i.e. the buyer's out-of-pocket expenditure) so the buyer's net price is s_iP_i.

The demand curve for each individual buyer is:

(1)
$$q_i = \frac{a_i - s_iP_i}{b}.$$

Let n_i be the number of buyers. Multiplying q_i in equation 1 by n_i gives the total quantity of the antimicrobial used in country i (Q_i) at a given price:

(2)
$$Q_i = n_i\left(\frac{a_i - s_iP_i}{b}\right).$$

where $Q_i = n_iq_i$. Solving for P_i, the demand for the antimicrobial becomes:

(3)
$$P_i = \frac{1}{s_i}\left(a_i - \frac{bQ_i}{n_i}\right).$$

MEB_i is the marginal external benefit. MEB_i exists because antimicrobial use decreases the risk of infecting others. One argument for a public health system is that users of antimicrobials are unlikely to take into account the external benefits of antimicrobial use since the benefits go to other people.

The marginal social benefit (MSB_i) is the vertical summation of the MEB_i and the demand curve:

(4)
$$P_i = a_i - \frac{bQ_i}{n_i} + MEB_i = MSB_i.$$

When calculating the optimal price and quantity, subsidies and taxes are not included, thus s_i is not included in equation 4.

MC_i is the marginal cost of an antibiotic treatment in country i. MC_i includes not only the price of the antibiotic but also the cost of visiting the doctor to get a prescription, the inconvenience and discomfort of complying with the treatment, and the availability and ease of access to health care facilities. When patients can purchase antibiotics without a prescription, the cost of visiting the doctor can be ignored and the marginal cost decreases. The lack of regulation on the quality of drugs and the dispensation of drugs is a major problem especially in developing countries (Okeke et al., 1999). Also, the marginal cost decreases when there is easy access to nearby health care clinics and pharmacies (Walson et al. 2001).

A key determinate in antimicrobial resistance is the volume of antibiotic exposure (Austin et al. 1999; Levin et al. 2000; and Arason et al. 1996). Countries that use more antibiotics tend to have more resistant bacteria (Bronzwaer et al., 2002 and Costelloe et al., 2010). This implies that the marginal external cost (MEC_i) increases with antimicrobial exposure. When there is no antibiotic use, MEC is zero. As antibiotic use increases, MEC also increases. The marginal social cost (MSC_i) is the vertical summation of the marginal cost and the marginal external cost i.e. $MSC_i = MC_i + MEC_i$.

This is illustrated in Figure 1. With no intervention and multiple producers of the antibiotic, a competitive market will produce at point A with a price of P and Q treatments. The efficient quantity of antimicrobial treatments is at point B where $D+MEB=MC+MEC$ and is denoted Q^* with a price of P^*. Current concern about antibiotic resistance implies that the MEC is much larger than the MEB. Thus, antibiotic treatments are reduced in Figure 1.[3]

There are likely to be major disagreements on the optimal level of antibiotic treatment. The economically efficient level of antibiotics is probably greater than the medically efficient level (Rubin, 2004-2005). This is because calculations of medical efficiency may ignore the value that patients place on avoiding the costs from additional visits to the doctor when the diagnosis is uncertain. On the other hand, public health officials have an incentive to overstate the effects of resistance to gain access to more resources (Best, 2005).[4] If public health officials overestimate the costs of resistance then they may try to reduce the level of treatments too much.

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[3] Though straight lines are used for ease of exposition, the *MEC* curve is likely to start out at fairly low levels and then increase at increasing rates. Likewise, the *MEB* instead of being constant probably tends to diminish as more antibiotic treatments are used.

[4] Best (2005) illustrates how statistics are often inflated or selectively highlighted by usually sincere advocates to gain media attention and resources. This may cause too many resources to be allocated to reduce antibiotic resistance.
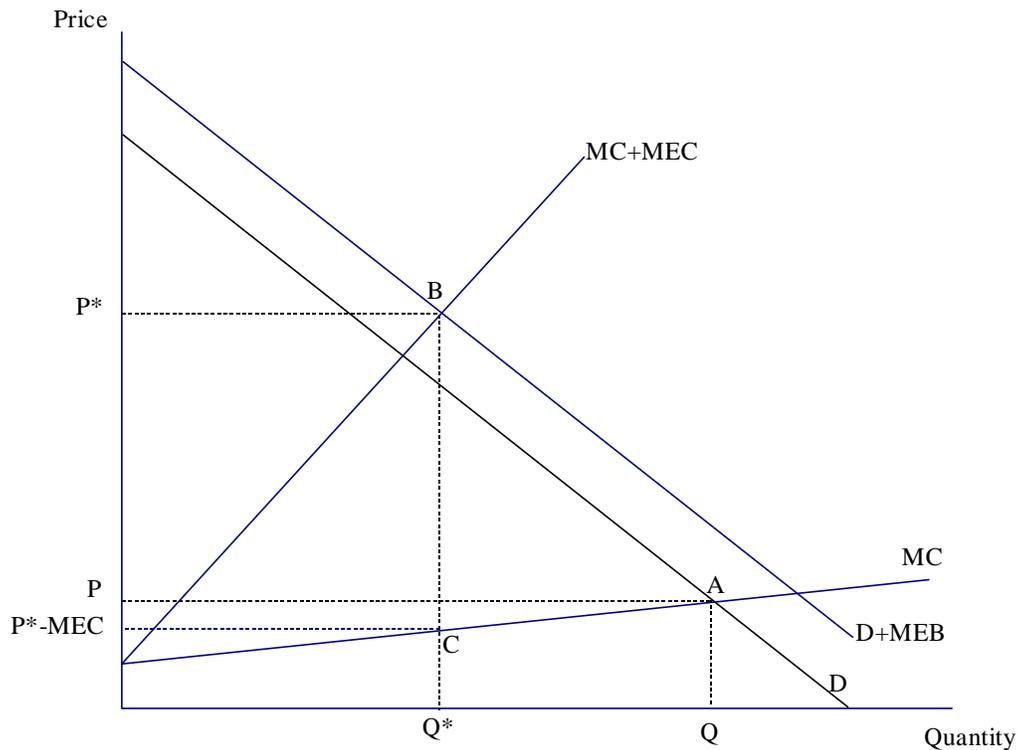
Figure 1
Efficient Use of the Antibiotic

How economic development affects communicable diseases

Looking at diseases for which antibiotics are commonly prescribed, the burden of disease is about 61 times higher in low and middle income countries than in high income countries (Mathers et al. 2006).[5] Since eighty-five percent of the world's population lives in low and middle income countries (CIA World Factbook, 2006), adjusting for population, the burden of disease is about 11 times higher in low and middle income countries than in high income countries.[6] In other words, high income countries have about 9.1% (1/11) of the disease burden that low and middle income countries have.

Part of the reason for more infections in the developing world is because of crowding in urban areas and lack of sanitation. Economic development is normally accompanied by internal migration and increased population density (Todaro, 1969). As people migrate to cities, microbial resistance to antibiotics may increase. This is because living in crowded unsanitary living conditions makes it easier to transmit resistant bacteria and people living in urban areas

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[5]   These calculations include tuberculosis (TB), Sexually Transmitted Diseases (STDs), diarrheal diseases, pertussis, diphtheria, tetanus, meningitis, leprosy, and respiratory infections. However, some of these diseases such as respiratory infections are caused by viruses. Mathers et al (2006) also combine low income and middle income countries into one category and calculate Disability-Adjusted Life Years (DALY) to quantify the global burden of disease.

[6]   Authors' calculations using data from Mathers et al (2006).

usually have easier access to antibiotics. Nys et al. (2004) found that in eight developing countries, *faecal E. coli* resistance was higher in urban populations than rural populations.

Throughout the world, urban areas gain approximately 67 million people per year or about 1.3 million per week (Meeting the Urban Challenge 2002). A major component of this increase is because rural people are attracted to cities in search of higher expected incomes (Todaro 1969, Meeting the Urban Challenge 2002). Even though the average health of urban residents is higher than that of rural residents, the living conditions of the urban poor are worse than those of the urban non-poor and are often worse than conditions of the rural poor. In 2005, 31.2 percent of the world's urban population lived in slums (State of the World's Cities 2006/7); This represents more than a billion people. The urban poor who are especially at risk live in crowded conditions, with poor sanitation, and unsafe water.[7] Polluted water and inadequate sanitation increase the probability of contracting diseases.[8]

This is analogous to nineteenth century America where internal migration caused as much as 50 percent of the increase in measured per capita income in the antebellum era (Fogel 2004). Internal migration, however, also was a major factor in spreading diseases such as cholera, typhoid, typhus, malaria, and dysentery (Smillie 1955 and Fogel 2004). Increased density also increased the prevalence of malaria, enteric diseases, and diseases of the respiratory system (Smillie 1955, May 1958, and Fogel 2004).

As countries continue to develop, however, the number of microbial diseases falls dramatically. For example, since the 18th century, there has been a long-term decline in infectious disease mortality in developed countries (McKeown, 1976; Kunitz, 1991; Woods, 1991; and Riley & Alter, 1989). Reductions in infectious diseases increases the proportion of ingested energy available to work since less energy is used to mobilize the immune system (Dasgupta, 1993). The capacity of the gut to absorb nutrients improves especially when there are fewer diarrheal diseases (Dasgupta, 1993). The reduction in infectious diseases in developed countries was caused by improvements in nutrition, pasteurization, public hygiene, health care, vaccinations, and draining swamps (McKeown, 1976; Kunitz, 1991; Woods, 1991; Riley & Alter, 1989; Schofield and Reher, 1991; and Fogel, 2004).

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[7]   Households in developing countries often have limited access to improved sanitation and clean water supplies. Fifty-four percent of households in low income countries and 41 percent in middle income countries did not have access to improved sanitation and 24 percent of households in low income countries and 19 percent in middle income countries did not have access to clean water sources in 2000 (World Development Indicators 2001). In developed countries, almost everyone had access to improved water sources and sanitation.

[8]   Cholera is mainly transmitted through contaminated food and water and is usually limited to developing countries where clean water and adequate sanitation are relatively scarce (Sack et al. 2001). Shigellosis is primarily a disease of poor and crowded communities that do not have adequate sanitation or safe water (Sack et al. 2001). In the developing world, shigellosis primarily infects children, with the urban poor being most affected. Fatality rates are highest among children less than five years of age, especially those who are malnourished. Most *Campylobacter* infections are through ingestion or handling of raw or inadequately prepared poultry, drinking raw milk, drinking contaminated water, and through fecal contact (Sack et al. 2001). There is also strong evidence that *Campylobacter* infections may be a major cause of Guillain-Barre syndrome (Allos, 1998). In the United States, about 40 percent of Guillain-Barre Syndrome cases previously had *Campylobacter* infections (Altekruse et al. 1999). In developing countries, some cases of Guillain-Barre Syndrome probably were mis-diagnosed as polio. With the reduction in polio, many more cases of Guillian-Barre Syndrome will probably be diagnosed. Though, *Campylobacter jejuni* is the most common cause of diarrheal illness in the United States, *Campylobacter* infections are relatively rare in industrialized countries (Sack et al. 2001).

Though developing countries have more infectious diseases than developed countries, following the Second World War, better nutrition, clean water supplies, improved sanitation, pasteurization, and vaccinations helped reduce infectious disease mortality in many developing countries (World Bank, 1993). However, unlike the reduction in infectious diseases in the United States and Europe, medical interventions such as oral rehydration therapy, immunizations and antibiotics played a major role in reducing mortality in developing countries (Gwatkin, 1980; Hill and Pebley, 1989; and Ruzicka and Kane, 1990). Still, in less affluent countries that lacked public health infrastructure, increased urbanization led to crowded unsanitary conditions that caused more communicable diseases (Mutatkar, 1995).

Many of these medical interventions were financed by foreign aid. Foreign aid may have contradictory results on microbial resistance to antibiotics. Programs that increase access to antibiotics either by establishing clinics or subsidizing antibiotic purchases tend to increase resistance. For example, Walson et al. (2001) found that people who lived closer to clinics in Nepal had more resistant bacteria. On the other hand, programs that reduce microbial infections tend to reduce antibiotic use and thus resistance.

Gottret and Schieber (2006) note that foreign aid is often used to provide medical services to the non-poor even though it was intended to provide medical services to the poor.[9] Gottret and Schieber (2006) also note that the foreign aid received is too small given the disease burden. Also, the amounts they do receive are hard to administer because the country may receive large amounts of foreign aid one year, then a much smaller amount the next year. When donations are reduced, reallocating funds to cover the lost donations is difficult.

One of the most effective ways to reduce resistance is to prevent microbial infections. Preventing microbial infections reduces n_i. Equation 3 shows that a reduction in n_i rotates the demand curve toward the origin along the quantity axis, but does not change the price intercept. This decrease in n_i can be shown in Figure 2 as a rotation from D to D'. Let D represent low and middle income countries and D' represent high income countries. Since high income countries have about 9.1% of the infectious disease burden per capita that low and middle countries have, then $n_i=1$ for demand curve D and $n_i=0.091$ for demand curve D'.[10] In Figure 2, the equilibrium number of antibiotic treatments for demand D is Q and the efficient quantity is Q^*. The equilibrium quantity for demand D' is Q' and the efficient number of treatments is Q'^*. For ease of presentation, at Q'^* the $MEB=MEC$ so that $Q'^*=Q'$.

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[9]   Foreign aid that is used to provide medical services to the non-poor even though it was intended to provide medical services to the poor is similar to a story told by Gordon Tullock where a fraudulent charity encourages people to help starving children. After collecting donations, the charity has professional actors pose in "before and after" photos showing the great benefits produced by the donations, and distributes the photos to the donors. This is Pareto optimal: the givers benefit, the charity becomes rich, and, assuming the donations were not diverted from a charity that would actually help the starving children, the real starving children are not hurt. When there is deception, Tullock argued that Pareto optimality can lead to policies that people would not support if they were better informed and exposing the fraud leads to the donors being worse off.

[10]   This assumes that people only buy antibiotic when they have an infectious disease and the only difference between high income countries and low and middle income countries is the number of buyers (n_i).

The demand for an antibiotic can also be reduced by substituting other currently existing antibiotics, newly discovered antibiotics or other substances with antimicrobial properties such as plants like garlic (Ankri and Mirelman, 1999), phage therapy (McGrath and van Sinderen 2007), sulfa drugs, or even anti-oxidants (Galley et al. 1997).[11] However, unlike reducing microbial infections which rotates the demand curve in toward the origin, substitutes reduce a_i in equation 3 which causes a parallel decrease in demand. Decreasing the demand for the antibiotic decreases the equilibrium quantity of the antibiotic and the equilibrium price.
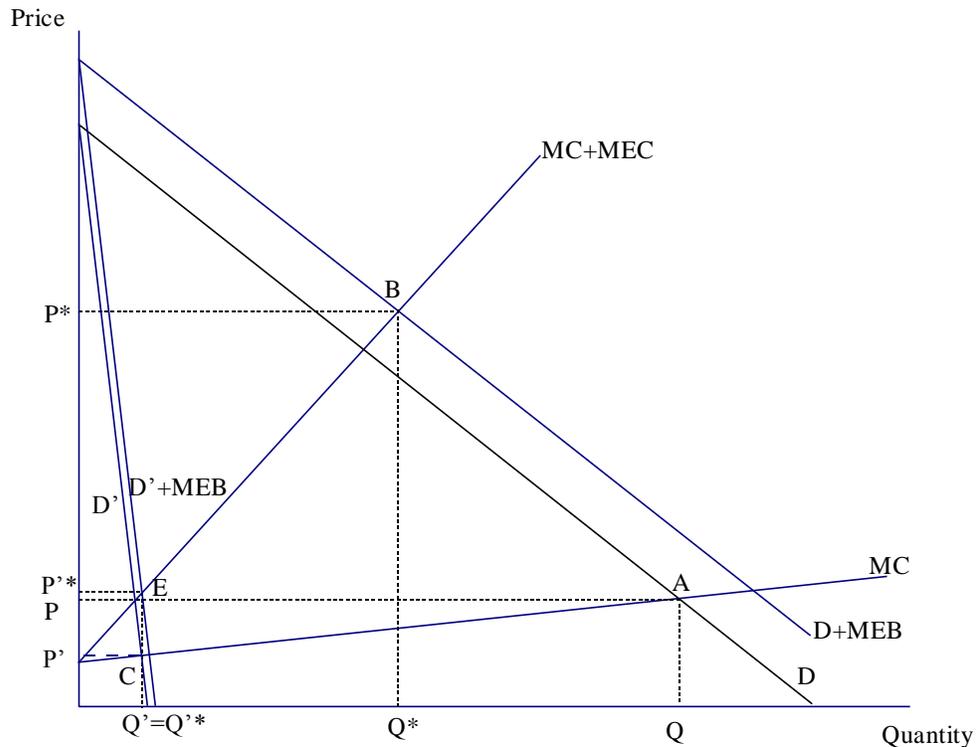
Figure 2
Prevention decreases the demand
for Anti-microbials

How higher incomes and lower out-of-pocket expenditures affect the demand curve.

Figure 3 illustrates the effect of higher incomes for low (D_l), middle (D_m), and high (D_h) income countries. Income increases dramatically as countries develop.[12] In 1999, Gross National Income (GNI) per capita was $1,870 for poor countries, $5,200 for middle income countries, and $25,690 for high income countries (World Development Indicators, 2001).[13]

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[11]   Palaniappan and Holley (2010) find that natural antimicrobials may also have a synergistic effect with antibiotics by increasing the antibiotic susceptibility of drug resistant bacteria.

[12]   In each country, the antibiotic is assumed to be a normal good and *b* is assumed to equal 1. Istúriz and Carbon (2000) report that in some low income countries per capita health expenditures are less than $10. However, living standards in the low income country are probably understated because low income countries tend to have more home production, underground markets, and barter transactions.

[13]   These figures use purchasing power parity.

Income per capita is about 178 percent (($5,200-$1,870)/$1,870) more in middle income countries than low income countries. Income per capita in the high income countries is about 394 percent (($25,690-$5,200)/$5,200) higher than in the middle income countries and 1274 percent (($25,690-$1,870)/$1,870) higher than in the low income countries. Baye et al. (1997) estimated that the income elasticity for anti-infectives was about 1.331. Holding everything else constant, the GNI figures and the 1.331 income elasticity, imply that middle income countries will use 237 percent (1.78*1.331) more antimicrobials than low income countries and high income countries will use 1,696 percent (12.74*1.331) more antimicrobials than low income countries.[14]

Figure 3
Higher Incomes Increase the
Demand for Anti-microbials

In the example in Figure 3, D_m and D_l are added to Figure 1 to illustrate how large an effect higher incomes along with the income elasticity can have on the demand for antibiotic treatments.[15] With increasing incomes, consumers tend to decrease the percentage of their out-of-

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[14] These GNI and the income elasticity numbers may only apply to a specific period of time and thus may not be generalizable to other times or situations.

[15] However, improvements in nutrition and physiology were major contributors to economic development. In 1790, people in the bottom 20 percent of caloric consumption in England and France probably did not have enough energy for sustained work and were thereby effectively excluded from the labor force (Fogel, 2004). Even those in the work force probably had only enough energy for limited amounts of work. Since then the number of calories available each day increased by about 50 percent (Fogel, 2004). This increase in calories gave the bottom 20 percent enough energy to enter the work force and increased the productivity of people already in the work force. Part of this increased productivity is because when people have better clothing and shelter there is less energy lost through the radiation of body heat (Dasgupta, 1993) and because the composition of diets shifted from grains and

pocket expenditures on health care (Gottret & Schieber 2006). In low income countries, more than 60 percent of health care expenditures are out-of-pocket. Out-of-pocket expenditures fall to 40 percent in middle income countries and 20 percent in high income countries (Gottret & Schieber 2006).

Figure 4 shows the effect of lower out-of-pocket expenditures on the demand curve. $D_{1.00}$ shows the previous demand curve where all expenses are paid by the purchaser of the antibitotic treatment. $D_{0.60}$ is for patients who pay 60% of the cost of their treatment, $D_{0.40}$ is for patients who pay 40%, and $D_{0.20}$ is for patients who pay 20% of their treatment. The original equilibrium point is at A and the efficient output is a point B. Now that people are receiving a subsidy to purchase the antibiotic the new equilibrium point is at C where people are willing to pay a higher price since someone else is paying and output is at Q'. Lower out-of-pocket expenditures give people an incentive to consume more antibiotic treatments.

When countries grow from low income to middle income countries, out-of-pocket health expenditures drop by 50 percent ((.4-.8)/.8). When countries grow from middle to high income countries, there is a similar 50 percent ((.2-.4)/.4) drop in out-of-pocket health expenditures. As mentioned above, Baye et al (1997) calculated the uncompensated price elasticity of demand for anti-infectives to be about -0.916. Everything else constant, given the 50 percent reduction in out-of-pocket expenditures as a low income country develops to a middle income country,

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other foods with high fiber content to meats and sugars with a higher proportion of ingested energy that could be metabolized (Fogel, 2004). Fogel (2004) estimates that this "thermodynamic" factor accounts for about 30 percent of the English growth rate since 1790.

there may be nearly a 46 percent (-0.916*0.5) increase in antibiotic purchases and another 46 percent (-0.916*0.5) increase in purchases as countries develop from middle income to high income countries.

Because of low incomes and high out-of-pocket expenditures, many poor patients in low income countries buy a small amount of an antibiotic and quit using it once symptoms disappear rather than after the treatment is complete (Okeke et al. 1999).[16] Not completing a treatment may select for more resistant bacteria.

On the other hand, treatment guidelines may recommend long durations of treatment when short courses of treatment may not only be effective, but also reduce antibiotic exposure (Paul, 2006). In mild to moderately severe cases of community acquired pneumonia, El Moussaoui et al. (2006) suggest that the appropriate duration of antibiotic treatment is three days rather than the recommended eight days.

Though economic development tends to decrease the percentage of people's incomes spent on antibiotics, the effect of this decrease on microbial resistance to antibiotics is ambiguous. If people in developed countries are more likely to complete antibiotic treatments, then economic development may reduce microbial resistance. On the other hand, if people are more likely to consume antibiotics because the relative price falls, then economic development may increase microbial resistance. The next section discusses how higher incomes, lower out-of-pocket spending and fewer communicable diseases affect human antibiotic use.

Figure 4
Lower Out-of-Pocket Spending
Increases the Demand
for Antimicrobials

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[16] This implies that policies that require patients to buy the full course of the antibiotic rather than by the tablet help reduce the premature stoppage of treatment.

How higher incomes, lower out-of-pocket spending, and fewer infections affect antibiotic treatments.

To estimate the magnitude of the effects of economic growth on the number of antibiotic treatments, consider how infections, out-of-pocket spending, and income affect the number of antibiotic treatments. Column 2 in Table 1 shows that the high income countries have 9.1% of the infections of low and middle income countries. Column 3 shows that out-of-pocket spending is 60% the low income countries, 40% in the middle income countries, and 20% in the high income countries so s_l=0.6, s_m=0.4, and s_h=0.2.

Table 1 How infections, out-of-pocket spending and income affect the demand for antibiotic treatments			
Country (1)	*n* (2)	*s* (3)	*a* (4)
High Income	*0.091*	*0.2*	*16.96*
Middle Income	*1*	*0.4*	*2.37*
Low income	*1*	*0.6*	*1*

As shown in Column 4, assuming antibiotics are normal goods, increasing income increases the demand for antibiotics. Holding everything else constant, higher incomes and the income elasticity of demand may cause middle income countries to demand 2.37 times more antibiotic treatments than low income countries and high income countries to demand 16.96 times more treatments than in low income countries.[17]

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[17]   This assumes that the availability and prices of substitutes are equivalent in each country.

Figure 5 illustrates the net effects of higher incomes, lower out-of-pocket spending, and fewer people infected with microbial diseases. Assuming $b=1$, D_l is the demand curve for the low income country, D_m is the demand curve for the middle income country and D_h is the demand curve for the high income country. The middle income country has a larger demand (D_m)

Price

D_h

D_m

D_l

MC

Q_l Q_h Q_m Quantity
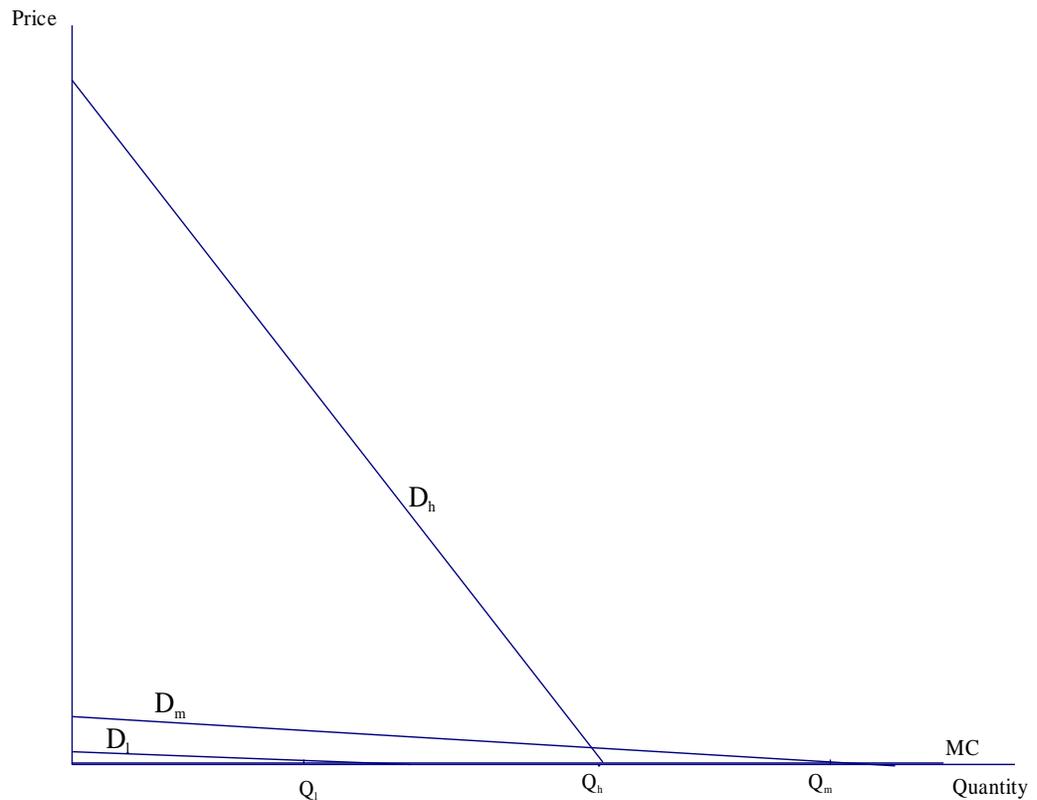
Figure 5
How Economic Growth Affects the
Demand for Anti-microbials

than the low income country (D_l), because people can afford to buy more antibiotics, the government has a larger budget to provide antibiotics, and out-of-pocket health expenditures decrease. The net effect on demand of developing from a middle income to a high income country is shown by shifting the demand curve from D_m to D_h. There are two reasons for this shift. First, the high income country has more than 10 times more income than the middle income country so a_h is more than ten times larger than a_m and second, the high income country has less than a tenth of the infectious diseases of the middle income country so n_h is less than a tenth of n_m. The increase in a_i causes a parallel shift to the right of the demand curve and the decrease in n_i causes the demand curve to rotate to the left but did not change the vertical price intercept.

In middle income and high income countries, the *MC* is likely to be lower than in low income countries because of improved storage and transportation systems. However, for simplicity in Figure 5, assume that the *MC=$1* for each country.

These inferred demand curves and the assumed marginal cost curve imply that, at first, economic growth increases microbial treatments (Q_l to Q_m) and increases antibiotic resistance.[18] However, further economic growth (Q_m to Q_h) reduces antibiotic treatments.[19]

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[18]   The speculated increase from Q_l to Q_m is because of the number of infectious diseases in developing countries, the higher incomes in middle income countries than in low income countries and the lower out of pocket

In Figure 5, patent protection is likely to reduce antibiotic sales much more in the middle income country than in the high income country. On the other hand, the price for patented antibiotics is likely to be much higher in the developed country than in the middle income country. Since patented drugs are likely to be less available in developing countries, they are less likely to increase microbial resistance than generic drugs while microbial resistance against patented drugs is more likely to appear in richer countries.

Figure 6 compares the optimal level of antibiotic treatments with the quantities of antibiotics people wish to purchase. D_l*, D_m*, and D_h* are the demand curves for the low, middle, and high income countries respectively when all expenditures for the antibiotic are out-of-pocket ($s_i=1$).
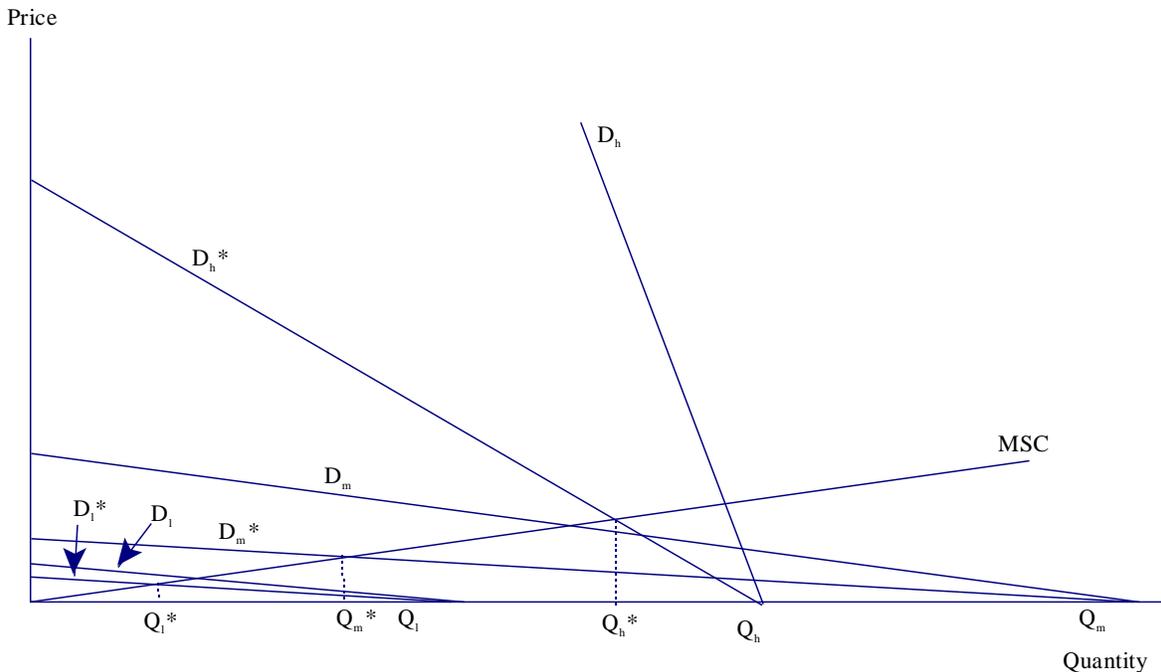
Figure 6
How the MEC affects the Effcient
Use of Antibacterial Treatments

The quote at the beginning of this article from the World Health Organization implies that antibiotic resistance has a significant effect on the optimal level of antibiotic treatments.[20]

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expenses in the middle income countries.

[19]   The speculated decrease from Q_m to Q_h is mainly because the large decrease in infectious diseases reduces the demand for antibiotics.

[20]   According to Roberts et al. (2008) antibiotic dosing depends not only on the bacteria isolated but also the most resistant bacteria. Thus preventing further resistant infections may be achieved by increasing antibiotic exposure to the highest recommended dose.

MSC is chosen as representative of fairly large effects from antibiotic resistance. Assuming for simplicity that *MEB*=0, Q_l^*, Q_m^*, and Q_h^* are the optimal treatments for the low, middle and high income countries respectively. The optimal number of treatments is highest for the high income country followed by the middle income country. The low income country has the lowest amount of optimal treatments.

Figure 6 implies that countries with the greatest burden of disease would require the largest reductions in antibiotic use. However, withholding antibiotics from those most in need creates serious ethical issues.

Evidence on Economic Growth and Microbial Resistance

A major issue with respect to microbial resistance is the scarcity of data, particularly from developing countries.[21] The little available data are disease specific and under-represent developing countries. Global studies include one or two developing countries or none at all. Combining data from different studies is problematic because the methodology is not standardized.

A global study that included some developing countries is Stelling et. al. (2005). That study integrated *Escherichia coli* antimicrobial susceptibility data from multiple surveillance programs. Table 2 shows 2001 non-susceptibility rates of *Escherichia coli* by income level. There are eighteen high income countries, eight upper-middle income countries, three lower-middle-income economies, and zero low-income economies included in these calculations.[22] As shown in column 1, Stelling et al (2005) present non-susceptibility rates for four antimicrobials: ampicillin, trimethoprim/sulfamethoxazole, ceftazidime, and ciprofloxacin. The percentages in column 1 are the non-susceptible rates for each drug. Lower percentages mean less microbial resistance.

For every drug in Table 2, as income increases, there is less microbial resistance. Consider resistance rates for ampicillin. In high income economies, 22% have non-susceptibility rates between 20-40%, 56% have non-susceptibility rates between 40-60%, and 22% have non-susceptibility rates greater than 60%. In upper-middle income economies, half have non-susceptibility rates for ampicillin between 40-60% and half have non-susceptibility rates greater than 60%, while in lower-middle-income countries, all had non-susceptibility rates greater than 60%. Since no low-income countries were included, dashes represent the absence of data.

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[21]   Antimicrobial use data are much more unreliable than resistance data because of unofficial supply chains in developing countries that cannot be quantified.

[22]   Income classifications are based on World Bank definitions. The high income countries include Australia, Belgium, Canada, Czech R., France, Germany, Greece, Hong Kong, Ireland, Israel, Italy, Japan, Singapore, Spain, Sweden, Switzerland, United Kingdom, and the United States. High-middle-income countries include Argentina, Brazil, Chile, Mexico, Poland, South Africa, Turkey, and Venezuela. Low-middle-income countries include Colombia, Philippines, and Thailand. Taiwan was not included since the World Bank income categories don't include Taiwan. The data for Thailand only includes the drug Ceftazidime.

Drug	High-income economies (18)	Upper-middle income economies (8)	Lower-middle-income economies (3)	Low-income economies (0)
Ampicillin				
20-40%	22%	0%	0%	-
40-60%	56%	50%	0%	-
>60%	22%	50%	100%	-
Trimethorim/ sulfamethoxazole				
0-20%	17%	0%	0%	-
20-40%	56%	38%	0%	-
40-60%	28%	63%	100%	-
Ceftazidime				
≤5%	89%	63%	0%	-
>5%	11%	38%	100%	-
Ciprofloxacin				
≤10%	61%	40%	0%	-
>10%	39%	60%	100%	-

*Table 2: Non-susceptibility rates of Escherichia coli by income level, 2001**

*Authors' calculations from Table 3 in Stelling et al (2005).

Conclusion

Stelling et al. (2005) show that developing countries have more antibiotic resistance than developed countries. Three reasons why developing countries tend to have more resistance to antibiotics are: First, poverty and high out-of-pocket health expenditures in developing countries give consumers an incentive to purchase antibiotics in small quantities and stop treatment prematurely when their symptoms stop, thereby eliminating the less resistant bacteria while leaving the more resistant bacteria to multiply. Second, poverty and migration to cities increases the number of people living in crowded unsanitary conditions which increases infectious diseases. And third, people living in urban areas have easier access to antibiotics.

As economic development continues and incomes increase, infections decline with the advent of clean water supplies, effective sanitation systems, better public health, improved housing, better clothing, improved nutrition, pasteurization, vaccinations, drained swamps and better educated health care workers and consumers.[23] Reducing infectious diseases increases the proportion of ingested energy available to work since less energy is used to mobilize the immune system and the capacity of the gut to absorb nutrients improves, especially when there are fewer diarrheal diseases. The decline in infectious diseases creates a benefit to non-infected people since they are less likely to become infected. As infections decline, fewer people use antibiotics and the growth rate of microbial resistance to antibiotics decreases.

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[23] According to Easterlin et al (2011) economic growth causes people at first to migrate to cities because of the better living conditions but as countries continue to develop rural conditions improve.

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P

D_m

D_l

A

MC

D_h+MEB

D_h

Q^*

Q

Quantity

Figure 3
Higher Incomes Increase the
Demand for Anti-microbials
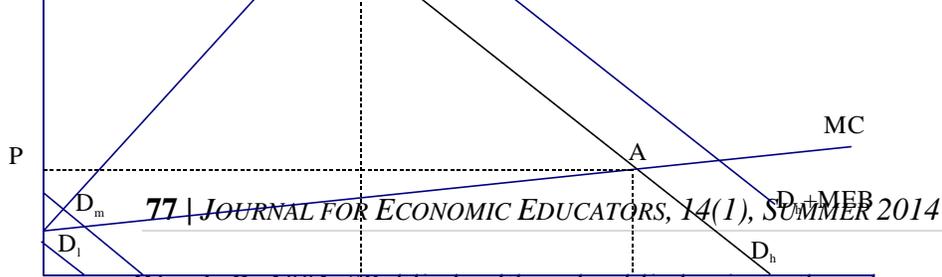
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