

High cost burden and health consequences of antibiotic resistance: the price to pay

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Abstract

Introduction: Rising antibiotic resistance may negatively affect the health and cost of care for patients. This study aimed to determine the impact of antibiotic resistance on costs and health consequences for patients.

Methodology: A one-year observational study was conducted at Christian Medical College, Vellore, a tertiary care hospital, on patients admitted into medical wards with a preliminary diagnosis of suspected sepsis. Patients with confirmed bacteremia were analysed in two groups – resistant and susceptible – based on susceptibility of causative bacteria to the empiric antibiotics administered. Clinical data and details about costs incurred were collected from hospital records. Costs and health consequences were compared using Mann-Whitney U test and Fisher's exact test. For median difference in costs, 95% bootstrap confidence interval was determined.

Results: Overall, 220 patients were included. The median difference between resistant and susceptible groups in overall costs, antibiotic costs, and pharmacy costs was rupees (INR)/USD 41,993/700 ($p = 0.001$), 8,315/139 ($p < 0.001$) and 21,492/358 ($p < 0.001$), respectively. Health consequences such as intensive care admissions, complications, mortality, and length of stay were significantly higher in the resistant group as compared to susceptible group: 44% vs. 21% ($p < 0.001$), 56% vs. 37% ($p = 0.006$), 12% vs. 2% ($p = 0.011$), and 14 vs. 11 days ($p = 0.027$), respectively.

Conclusions: Antibiotic resistance has a significant impact on cost and health consequences. These findings provide a key message for policymakers and other stakeholders to initiate feasible strategies to tackle resistance and reduce the burden.

Key words: antibiotics; antimicrobial resistance; economic burden.

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Introduction

Antibiotic resistance is rising and is a truly global problem [1,2]. It has reached alarming proportions in low- and middle-income countries (LMICs) such as India [3,4]. Resistance is closely associated with antibiotic pressure at individual and aggregate levels [5,6]. Inappropriate use of antibiotics in infections has been well documented [7]. Many older-generation antibiotics have become less effective against bacteria [8]. In response, newer antibiotics have been prescribed that are significantly more costly [9]. The impact on patient outcomes and on health systems need to be closely assessed, especially in LMICs.

Government health centers have been the main facilities for healthcare in India. There has been a deterioration of services over the years [10,11].

Currently, mainly the poor utilize these facilities. Budget constraints necessitate stocks of inexpensive, older-generation antibiotics such as cotrimoxazole. Other antibiotics are often unavailable [7]. Due to poor infrastructural facilities, many patients have increasingly turned to the private health sector [11]; this has increased direct costs. Current estimates suggest that medicines account for 72% of families' out-of-pocket (OOP) health expenses [12].

It is therefore imperative to determine the incremental cost burden to patients if causative bacteria are resistant to empiric antibiotics. A loss of valuable time and grave health consequences may result, especially in severe bacterial infections. The switch to more effective and newer antibiotics may increase expenses. Studies on the impact of antibiotic

resistance in individual patients are lacking, especially from LMICs. With this purpose, a study was conducted on hospital in-patients with a preliminary diagnosis of suspected sepsis and confirmed bacteremia to assess the direct cost burden and health consequences of resistance to the empiric antibiotic administered.

Methodology

Design and setting

An observational study describing costs and health consequences was conducted at Christian Medical College (CMC), a tertiary care, not-for-profit university teaching hospital situated in Vellore, south India. This hospital, having 2,140 beds and more than 6,000 outpatients per day, caters to patients from various economic backgrounds and geographical locations in India [13]. The hospital has basic and higher speciality departments with more than ten intensive care units. This study was done in the medical wards and medical intensive care unit. The study is reported in accordance with the strengthening and reporting of observational studies in epidemiology (STROBE) guidelines [14].

Participants, variables and data collection

Participants were included based on the following criteria: (i) adult in-patients admitted into medical wards between 1 January and 31 December 2010 with a preliminary diagnosis of suspected sepsis; (ii) patients prescribed empiric antibiotic therapy; and (iii) blood culture report identifying causative bacteria with antibiotic susceptibility profile. The main outcome parameter was overall direct cost in rupees (one US dollar = 60 rupees) [15]. Various categories of costs incurred by the patients were documented. These were costs of antibiotics, the total cost of pharmacy items (medicines and consumable items), laboratory costs (investigations), and ward costs (all other costs incurred while in the ward). Overall costs included pharmacy (including antibiotics), ward, and investigation costs. Hospital electronic accounting records and the pharmacy database were used to determine these costs. The secondary outcome parameters were length of stay in hospital, intensive care admissions, complications, and mortality. This information was collected from patients' charts and electronic records. Data access and availability was good due to the comprehensive nature of data filing. Triangulation through these sources was done to maintain accuracy.

Resistance assessment

As part of the normal diagnostic work-up, patients admitted with a preliminary diagnosis of suspected sepsis had 5 to 8 mL of blood collected aseptically. Bedside inoculation was done in Bact-Alert bottles (bioMérieux, Marcy l'Etoile, France). Only aerobic bottles containing Trypticase soy broth were used. Bact-Alert bottles were loaded in Bact/ALERT3D system until a positive signal was identified, and characterized further using the Vitek2 system [16]. Samples were ruled negative if no signal was identified after five days of incubation. Bacterial resistance was assessed by antibiotic susceptibility testing performed on isolates by the Kirby-Bauer disk diffusion method at the microbiology department. This department operates the quality assessment program for microbiological laboratories in India under the umbrella of Indian Association of Medical Microbiologists. The susceptibility breakpoints for each drug are defined according to Clinical Laboratory Standards Institute (CLSI) guidelines [17]. The clinical pharmacology unit of the hospital randomly conducts content testing of antibiotics using high performance liquid chromatography.

Procedure and analysis

Patients with a preliminary diagnosis of suspected sepsis and receiving empiric antibiotic therapy were categorized into two groups: (i) the resistant group – all patients in whom the susceptibility report documented resistance of causative bacteria to the empiric antibiotic, and (ii) the susceptible group – all patients in whom the report documented susceptibility of causative bacteria to the empiric antibiotic. Empiric choices in the guidelines for suspected infections were based on local antibiograms. Empiric antibiotics were retained or changed based on the susceptibility report and clinical response. Antibiotics were coded based on the ATC (Anatomical, Therapeutic and Chemical) Index [18].

Overall and categorized costs incurred by patients in each group were compared. Costs were compared in rupees using Mann-Whitney U test and presented as median costs and their respective inter-quartile ranges (IQR). The median differences between the groups and their 95% bootstrap confidence intervals (CIs) were calculated using R version 2.15.1 [19]. Besides costs, health consequences in the two groups were compared. Length of stay was analysed using the Mann-Whitney U test. The proportion of patients having complications, patients with intensive care admissions, and mortality in each group were compared using

Fisher's exact test. $P < 0.05$ was considered significant.

Ethical approval

Permission to conduct this study was granted by the Institutional Review Board of Christian Medical College, Vellore (IRB(EC)-ER-5-10-03-2010).

Results

Over a period of one year, from January to December 2010, a total of 33,897 blood cultures from the entire hospital were received by the microbiology laboratory, of which 2,264 had positive blood cultures with confirmed bacteremia. Among this, 409 blood cultures were from medical wards. Duplicate cultures, cultures without susceptibility profiles, and cultures belonging to patients who did not have a preliminary diagnosis of suspected sepsis were eliminated from the list. Finally, 220 patients who had a preliminary diagnosis of suspected sepsis with confirmed bacteremia and who were administered an empiric antibiotic were included in the study. These patients were divided into two groups –resistant and susceptible – based on the susceptibility of the causative bacteria to the empiric antibiotics administered.

The resistant and susceptible groups (Table 1) were comparable. The main co-morbidity was diabetes. Other co-morbidities were kidney disease, liver disease, and involvement of other systems.

Escherichia coli with resistance to empirically used piperacillin-tazobactam was the most common Gram-negative bacteria (Table 2). *Staphylococcus aureus* with resistance to empirically used cloxacillin was the most common Gram-positive bacteria.

There was a significant difference in cost (Table 3) between resistant and susceptible groups in the three main categories – overall cost, antibiotic cost, and total pharmacy cost.

Intensive care admissions, complications, and mortality were significantly higher in the resistant group (Table 4). The median length of hospital stay was also higher.

Discussion

In India, infections still contribute significantly to morbidity and mortality [20]. Antibiotics are frequently used in the community for many infections [7,21]. There are many factors that promote their use [22]. Whatever the factor, increased use contributes to increased resistance [5,6]. Effective antibiotics have

thus become a precious resource, especially in severe bacterial infections.

Baseline data (Table 1) shows 220 patients categorized into two groups based on resistance or susceptibility to empiric antibiotics. The baseline demographic parameters and bacteria cultured compared well between the groups. Potential confounders such as diabetes (the major co-morbidity) and the number of co-morbidities compared well.

The most common Gram-negative culture isolate in the resistant group was *Escherichia coli*. Many of these patients were empirically given piperacillin-tazobactam (Table 2). Resistance to third-generation cephalosporins, fluoroquinolones, and carbapenems were also noted. Non-fermenting Gram-negative bacteria (NFGNB) were the next most common Gram-negative culture isolates. These isolates were resistant to piperacillin-tazobactam, carbapenems (meropenem), ciprofloxacin, and aminoglycosides used empirically. This widespread resistance is of great concern and reflects the dire situation regionally and globally [1-3].

Cost burden

The median overall cost was significantly higher in the resistant group compared to the susceptible group (Table 3). The average daily wage of a rural male casual worker in India is approximately INR 95 (USD 1.6) [23,15]. The median difference amount of INR 41,993 (USD 700) incurred by patients in the resistant group equates to 442 days of wages spent. This financial loss of more than one year's wages contributes significantly to the cost burden. Very few studies have looked at direct costs of resistant infections to patients, and none were conducted in LMICs. In a study in United States on cost attributable to acute resistant infections, the extra cost burden was calculated at 21,018 dollars [24]. The burden in India is compounded due to lack of health insurance and rising OOP expenditure. The national poverty line is INR 816 (USD 13.6) per capita per month in rural areas and INR 1000 (USD 16.7) per capita per month in urban areas [25]. In India, 21.9% of the population is below the poverty line (BPL) [25]. For BPL patients, the extra cost burden due to a single episode of a severe bacterial infection could be insurmountable. It may substantially raise the 5% rate of Indian households that currently suffer catastrophic health expenditures [12].

Table 1. Description of demographics, co-morbidities, and bacteria cultured

n = 220	Resistant group n = 133	Susceptible group n = 87
Mean age with SD	52 years (\pm 17.3)	53 years (\pm 17.2)
Gender		
Male	86 (65%)	58 (67%)
Female	47 (35%)	29 (33%)
Co-morbidities		
Patients with co-morbidities	112 (84%)	76 (87%)
Patients with diabetes alone as co-morbidity	42 (32%)	33 (38%)
Mean number of co-morbidities per patient with SD	2.1 (\pm 1.3)	2.3 (\pm 1.5)
Bacteria cultured		
Gram-negative bacteria (GNB)	102 (77%)	66 (76%)
<i>Escherichia coli</i>	53	37
<i>Klebsiella pneumoniae</i>	4	7
NFGNB*	36	15
<i>Enterobacter</i>	1	3
Other GNB	5	4
Mixed GNB	3	0
Gram-positive bacteria (GPB)	24 (18%)	18 (21%)
<i>Staphylococcus aureus</i>	17	8
<i>Enterococcus</i>	4	4
<i>Streptococcus pneumoniae</i>	3	4
Group A beta haemolytic streptococcus	0	2
Mixed GPB/GNB	7 (5%)	3 (3%)

*Non-fermenting Gram-negative bacteria included *Acinetobacter baumannii* and *Pseudomonas aeruginosa*

Table 2. Bacteria isolated in the resistant group and main empiric antibiotics used to which resistance was documented

	Piperacillin- Tazobactam	Cefotaxime	Ceftriaxone	Ciprofloxacin	Gentamicin	Amikacin	Meropenem	Ertapenem
Gram-negative Bacteria (GNB)								
<i>Escherichia coli</i>	43	3	6	7	2	1	1	-
<i>Klebsiella pneumoniae</i>	3	1	-	-	1	1	1	-
<i>Enterobacter</i>	1	-	-	-	-	-	1	-
NFGNB*	18	5	-	8	9	2	16	3
	Benzyl Penicillin	Cloxacillin		Ciprofloxacin	Vancomycin			
Gram-positive bacteria (GPB)								
<i>Staphylococcus aureus</i>	-	17		9	-			
<i>Enterococcus</i>	2	-		1	1			
<i>Streptococcus pneumoniae</i>	2	-		1	-			

*Non-fermenting Gram-negative bacteria included *Acinetobacter baumannii* and *Pseudomonas aeruginosa*

- indicates that particular antibiotic was not used empirically in patients whose blood culture grew respective bacterial isolates subsequently

A significant proportion of OOP health expenditure in India is spent on medicines [12]. The antibiotic costs borne by patients in the resistant group were significantly higher – by INR 8,315 (USD 139) – than those of patients in the susceptible group (Table 3). Pharmacy costs (Table 3) were again significantly higher in the resistant group. This shows that antibiotic resistance may also lead to use of other medicines and consumables, thereby further adding to the costs.

Health consequences

Secondary outcomes such as intensive care admission, complications, and length of stay were also assessed (Table 4). Patients in the resistant group had to stay in the hospital an extra three days. A US study done on patients with hospital-acquired infections

reported a longer stay [26]. Longer bed stay has cost implications and may increase the risk of hospital-acquired infections. Bed occupation where availability is scarce may delay treatment for other patients waiting to be admitted.

A comparison of intensive care admissions showed 23% more admissions in the resistant group (Table 4). Another study showed similar results, with a 37% difference in intensive care admissions [24]. Crucial beds in intensive care maybe occupied, thereby denying care to other critical patients. In our study, the proportion of patients developing complications was 19% higher in the resistant group. Renal failure, respiratory failure, and circulatory shock were some of the common complications. In the few studies looking at health consequences, the focus was length of stay

Table 3. Comparison of direct costs between resistant (R) and susceptible (S) groups (n = 220)

Cost in INR/USD	Resistant group n = 133 Median cost INR/USD (IQR)	Susceptible group n = 87 Median cost INR/USD (IQR)	R&S difference Median cost INR/USD (Bootstrap 95% CI)	p value
Overall cost	88,686/1,478 (36,265 – 164,850)	47,380/790 (25,847 – 86,087)	41,993/700 (16,667 – 63,848)	0.001
Antibiotic cost	16,734/279 (6,722 – 27,853)	8,255/138 (3,799 – 13,560)	8,315/139 (4,953 – 10,859)	<0.001
Total pharmacy cost	39,482/658 (20,205 – 64,431)	16,309/272 (9,359 – 36,891)	21492/358 (8,950 – 29,001)	<0.001
Laboratory investigation cost	12,235/204 (4,452 – 22,309)	8,436/141 (4,035 – 16,278)	3,710/62 (136 – 7,033)	0.055
Ward cost	12,425/207 (7,543 – 20,925)	10,300/172 (7,419 – 16,090)	2,060/34 (-286 – 4,045)	0.108

Table 4. Comparison of health consequences between resistant (R) and susceptible (S) groups

Patients n = 220	Resistant group n = 133	Susceptible group n = 87	Difference between R and S groups	p value
Median length of stay in days (IQR)	14 (8.5 – 22.5)	11 (8 - 17)	3	0.027
Hospital stay in days (range)	2-108	3-60	23%	<0.001
Intensive care admissions	59 (44%)	18 (21%)		
Mortality	16 (12%)	2 (2%)	10%	0.011
Complications	75 (56%)	32 (37%)	19%	0.006
System wise complications				
Renal	29	18		
Circulatory	16	5		
Metabolic	3	4		
CNS	4	3		
Respiratory	6	2		
Renal & circulatory	9	-		
Renal & metabolic	2	-		
Renal & respiratory	2	-		
Respiratory & circulatory	1	-		
Others	3	-		

and mortality [24,26]. Complications have a cascading impact on overall costs and therefore need to be assessed.

Mortality was five times higher in the resistant group. The magnitude of difference is larger than was previously reported. In a study with 1,391 hospitalized patients, there were 70 deaths (5%), of which only half had a resistant organism [24]. Another study in intensive care found that the hazard ratio for discharge dead or alive when comparing sensitive and resistant organisms was close to one [27]. Both these studies were not done in LMICs. The relatively higher mortality in the resistance group in our study, therefore, needs to be noted.

The impact of resistance and the required response

Rising resistance and the fear of ineffective antibiotics may lead to treatment with prolonged courses of newer, broader, and more expensive antibiotics. This will raise the cost burden even further. Rising resistance could also mean delays in treatment and health consequences. Multi-pronged strategies are needed to tackle the problem of resistance. Strategies should include infection control, improvement of diagnostics, guideline development, continuing education, and regulation enforcement. Changing behaviour and empowering the public are also important. For this to happen, awareness programs and mass media campaigns would be useful. The findings of this study could provide a key message that would catch the attention of all stakeholders, raise awareness about resistance, and help improve appropriate antibiotic use.

Methodological considerations

This is one of the first studies in an LMIC looking at cost and health consequences of antibiotic resistance. The data generated mainly focused on direct costs, but gives crucial evidence on the huge impact of antibiotic resistance. This study provides the basis for a future economic study, where indirect and intangible costs could be measured. Unlike high-income countries, which have data pooled in electronic records and national registries, the data for this study had to be sourced through multiple channels including accounts, pharmacy, clinical, and laboratory departments. Our study included all organisms, whereas others – one in China that compared extended-spectrum beta lactamase-positive and negative infections in intra-abdominal infections [28] and one in Europe on bloodstream infections [29] – focused on a limited number of organisms.

Conclusions

The findings of this study demonstrate significantly higher costs to patients infected with resistant bacteria as compared to those infected with susceptible bacteria. Mortality, the greatest price that patients have to pay, was significantly higher, underlining the association of antibiotic resistance to a fatal outcome. Other health consequences were also significantly higher.

Overall, the message is clear and alarming. The economic and health burden of resistance can be devastating to individual patients and to health budgets. This burden will be felt more by patients in LMICs, such as India, with low health insurance coverage and high OOP expenditure. This key message needs to be disseminated to all stakeholders, individuals, health professionals, hospital administrators, policymakers, and society as a whole. We hope that this message encourages stakeholders to refocus their attention on the dangers of resistance and tackle the problem through feasible strategies for appropriate antibiotic use and infection control practices. These measures will hopefully decrease the cost burden to the individual and improve health in the society.

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References

1. Gagliotti C, Balode A, Baquero F, Degener J, Grundmann H, Gür D, Jarlier V, Kahlmeter G, Monen J, Monnet DL, Rossolini GM, Suetens C, Weist K, Heuer O; EARS-Net Participants (2011) *Escherichia coli* and *Staphylococcus aureus*: bad news and good news from the European Antimicrobial Resistance Surveillance Network (EARS-Net, formerly EARSS), 2002 to 2009. *Euro Surveill* 16 (11): pii=19819.
2. Ho J, Tambyah PA, Paterson DL (2010) Multiresistant Gram-negative infections: a global perspective. *Curr Opin Infect Dis* 23: 546-553.
3. Mathai E, Chandy SJ, Thomas K, Antoniswamy B, Joseph I, Mathai M, Sorensen TL, Holloway K (2008) Antimicrobial resistance surveillance among commensal *Escherichia coli* in rural and urban areas in Southern India. *Trop Med Int Health* 13: 41-45.
4. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, Chaudhary U, Doumith M, Giske CG, Irfan S, Krishnan P, Kumar AV, Maharjan S, Mushtaq S, Noorie T, Paterson DL, Pearson A, Perry C, Pike R, Rao B, Ray U, Sharma JB, Sharma M, Sheridan E, Thirunarayan MA, Turton J, Upadhyay S, Warner M, Welfare W, Livermore

- DM, Woodford N (2010) Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis* 10: 597-602.
5. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD (2010) Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and metanalysis. *BMJ* 340: c2096.
 6. Goossens H, Ferech M, Vander Stichele R, Elseviers M; ESAC Project Group (2005) Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 365: 579-587.
 7. Kumari Indira KS, Chandy SJ, Jeyaseelan L, Kumar R, Suresh S (2008) Antimicrobial prescription patterns for common acute infections in some rural and urban health facilities of India. *Indian J Med Res* 128: 165-171.
 8. Karageorgopoulos DE, Falagas ME (2009) New antibiotics: optimal use in current clinical practice. *Int J Antimicrob Agents* 34 Suppl 4: 55-62.
 9. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R (2009) Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *Lancet* 373: 240-249.
 10. Purohit BC (2004) Inter-state disparities in health care and financial burden on the poor in India. *J Health Soc Policy* 18: 37-60.
 11. Varatharajan D, Thankappan R, Jayapalan S (2004) Assessing the performance of primary health centres under decentralized government in Kerala, India. *Health Policy Plan* 19: 41-51.
 12. Shahrawat R, Rao KD (2012) Insured yet vulnerable: out-of-pocket payments and India's poor. *Health Policy Plan* 27: 213-221.
 13. Christian Medical College Vellore (2011) Christian Medical College Vellore Year Book Supplement 2010 - 2011. Available: <http://www.cmchvellore.edu/pdf/CMCYear2011.pdf>. Accessed 18 March 2013.
 14. von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP; STROBE Initiative (2008) Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 61: 344-349.
 15. XE (2014) XE Currency Converter Exchange Rate. Available: <http://www.xe.com/currencyconverter/convert/?Amount=1&From=USD&To=INR>. Accessed 31 March 2014.
 16. Biomerieux (2009) BacT/ALERT® 3D: Healthcare. Available: http://www.biomerieux-usa.com/servlet/srt/bio/usa/dynPage?doc=USA_PRD_LST_G_PRD_USA_6. Accessed 20 March 2013.
 17. Clinical and Laboratory Standards Institute (2014) CLSI Standards Center. Wayne, USA: CLSI. Available: clsi.org/standards. Accessed 20 March 2013.
 18. WHO Collaborating Centre for Drug Statistics Methodology (2013) ATC/DDD Index. Oslo: WHO. Available: http://www.whocc.no/atc_ddd_index. Accessed 22 March 2013.
 19. R Project (2011) The R Project for Statistical Computing. Available: <http://www.r-project.org>. Accessed 22 March 2013.
 20. Ministry of Health and Family Welfare, Central Bureau of Health Intelligence (2012) National Health Profile of India 2012. Available: <http://www.cbhidghs.nic.in/index2.asp?slid=1256&sublinkid=1163>. Accessed 25 March 2013.
 21. Chandy SJ, Thomas K, Mathai E, Antonisamy B, Holloway KA, Stalsby Lundborg C (2013) Patterns of antibiotic use in the community and challenges of antibiotic surveillance in a lower-middle income country setting: a repeated cross-sectional study in Vellore, India. *J Antimicrob Chemother* 68: 229-236.
 22. Chandy SJ, Mathai E, Thomas K, Faruqui AR, Holloway K, Lundborg CS (2013) Antibiotic use and resistance: perceptions and ethical challenges among doctors, pharmacists and the public in Vellore, South India. *Indian J Med Ethics* 10: 20-27.
 23. Government of India Ministry of Labour and Employment (2011) Second Annual Report to the People on Employment. Table 4.5: Average Daily Wage Rates (in Rs.) across different population groups and types of works. Available: www.dget.nic.in/publications/annualreportemployment2011.pdf. Accessed 25 March 2013.
 24. Roberts RR, Hota B, Ahmad I, Scott RD, Foster SD, Abbasi F, Schabowski S, Kampe LM, Ciavarella GG, Supino M, Naples J, Cordell R, Levy SB, Weinstein RA (2009) Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. *Clin Infect Dis* 49: 1175-1184.
 25. Government of India Planning Commission (2011) Press Notes on Poverty Estimates 2011-2012. Available: http://planningcommission.nic.in/news/pre_pov2307.pdf. Accessed 26 August 2013.
 26. Mauldin PD, Salgado CD, Hansen IS, Durup DT, Bosso JA (2010) Attributable hospital cost and length of stay associated with health care-associated infections caused by antibiotic-resistant gram-negative bacteria. *Antimicrob Agents Chemother* 54: 109-115.
 27. Lambert ML, Suetens C, Savey A, Palomar M, Hiesmayr M, Morales I, Agodi A, Frank U, Mertens K, Schumacher M, Wolkewitz M (2011) Clinical outcomes of health-care-associated infections and antimicrobial resistance in patients admitted to European intensive-care units: a cohort study. *Lancet Infect Dis* 11: 30-38.
 28. Hu B, Ye H, Xu Y, Ni Y, Hu Y, Yu Y, Huang Z, Ma L (2010) Clinical and economic outcomes associated with community-acquired intra-abdominal infections caused by extended spectrum beta-lactamase (ESBL) producing bacteria in China. *Curr Med Res Opin* 26: 1443-1449.
 29. de Kraker ME, Davey PG, Grundmann H; BURDEN study group (2011) Mortality and hospital stay associated with resistant *Staphylococcus aureus* and *Escherichia coli* bacteremia: estimating the burden of antibiotic resistance in Europe. *PLoS Med* 8: e1001104.

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