

Frank, Uwe; Kaier, Klaus

Working Paper

Dynamics between antibiotic drug use and resistance: An economic approach

Diskussionsbeiträge, No. 36

Provided in Cooperation with:

Research Center for Generational Contracts (FZG), University of Freiburg

Suggested Citation: Frank, Uwe; Kaier, Klaus (2009) : Dynamics between antibiotic drug use and resistance: An economic approach, Diskussionsbeiträge, No. 36, Albert-Ludwigs-Universität Freiburg, Forschungszentrum Generationenverträge (FZG), Freiburg i. Br.

This Version is available at:

<http://hdl.handle.net/10419/38841>

Standard-Nutzungsbedingungen:

Die Dokumente auf EconStor dürfen zu eigenen wissenschaftlichen Zwecken und zum Privatgebrauch gespeichert und kopiert werden.

Sie dürfen die Dokumente nicht für öffentliche oder kommerzielle Zwecke vervielfältigen, öffentlich ausstellen, öffentlich zugänglich machen, vertreiben oder anderweitig nutzen.

Sofern die Verfasser die Dokumente unter Open-Content-Lizenzen (insbesondere CC-Lizenzen) zur Verfügung gestellt haben sollten, gelten abweichend von diesen Nutzungsbedingungen die in der dort genannten Lizenz gewährten Nutzungsrechte.

Terms of use:

Documents in EconStor may be saved and copied for your personal and scholarly purposes.

You are not to copy documents for public or commercial purposes, to exhibit the documents publicly, to make them publicly available on the internet, or to distribute or otherwise use the documents in public.

If the documents have been made available under an Open Content Licence (especially Creative Commons Licences), you may exercise further usage rights as specified in the indicated licence.



DISKUSSIONSBEITRÄGE DISCUSSION PAPERS

Dynamics between antibiotic drug use
and resistance – An economic approach

Uwe Frank
Klaus Kaier

No. 36 – März 2009



Dynamics between antibiotic drug use and resistance – An economic approach

Uwe Frank

Department of Environmental Health Sciences, University Medical Center Freiburg

Klaus Kaier*

Department of Environmental Health Sciences, University Medical Center Freiburg and
Research Center for Generational Contracts, Freiburg University

Abstract

In Europe, the emergence and spread of antibiotic resistance (AMR) has become a serious public health threat. Rational antibiotic policy, combined with enforcement of infection control practices are key strategies to combat AMR in the hospital setting. Using time-series analysis, we calculated potential savings resulting from changes in prescribing behaviour and improved compliance with hand hygiene. According to our calculations, a saving of 14 € would be achieved by reducing use of third-generation cephalosporins by one defined daily dose and further savings of almost 60 € would be achieved by increasing hospital-wide use of alcohol-based hand rub by one litre.

Keywords: Economic model, Externality, Antibiotics use, MRSA

* **Corresponding author:** Kaier, Klaus; Department of Environmental Health Sciences, University Medical Center Freiburg, Breisacher Straße 115b, D-79106 Freiburg, Germany; Phone +49(0)761/270 8272, Fax +49(0)761/270 8253, Email klaus.kaier@uniklinik-freiburg.de

Introduction

In the past decades, antibiotic resistance (AMR) in pathogenic bacteria has been a growing problem both in Europe and worldwide. The race against resistance began soon after penicillin was developed. When with the emergence and spread of resistant organisms penicillin began to lose effectiveness, scientists dealt with the problem by developing methicillin, a synthetic penicillin; however, that agent, too, soon began to lose effectiveness.¹ Thus, new classes of antimicrobial agents were developed to replace methicillin. Now, as development has slowed down the effectiveness of antibiotics in general is beginning to decline.^{2,3}

From a public health perspective, the effectiveness of antibiotic agents in hospital settings may be seen as a natural resource that is (1) protected by infection control practices implemented to prevent cross-transmission of resistant bacteria and (2) exploited by the use of antibiotics. Antibiotic use gives antibiotic-resistant bacterial strains a comparative advantage to spread, resulting in a direct correlation between the volume of antibiotic consumption and the spread of resistance in hospital settings, as 3 recent studies using time-series analysis have shown.⁴⁻⁶

Studies using time-series analyses on a hospital-wide level have shown that temporal increases (decreases) in the use of some classes of antibiotics are followed by temporal increases (decreases) in the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA), the most prominent multi-drug resistant pathogen. Furthermore, these studies have also shown that infection control practices such as hand disinfection are able to decrease MRSA incidence.⁴⁻⁶

Loss of antibiotic activity as a direct result of antibiotic consumption can be modelled on the approach of a negative externality. According to this concept, the cost of resistance is considered to be a negative externality of antibiotic use.^{7,8} The study-objective was to determine the externalities of four classes of antibiotics which scientifically influence the occurrence of MRSA in hospital setting.⁵

Methods

The model

The externality determines the level of the cost of resistance that is caused by use of one defined daily dose (DDD) of a selected antibiotic. Therefore, knowledge of the extent to which an antibiotic may have contributed to the emergence of resistance and what costs are incurred by which type of resistant infection is imperative.

Following existing approaches, the probability of the failure of antibiotic treatment due to a resistant organism is termed R , while the additional cost of infections caused by resistant bacteria are represented by ΔV . The impact parameter between antibiotic use and the occurrence of resistance ε is called dose-response rate of drug use – drug resistance and may be described as the percentage change in the incidence of resistance following a 1% change in the level of antibiotic use.⁸ The externality E of the use of antibiotic q is then given by

$$(1) \quad E_q = \varepsilon_q R_q \Delta V,$$

where the negative externality is determined by the linear relationship between antibiotic use and the occurrence of resistance ε , the probability of the acquisition of a resistant infection R and the constant costs of an infection caused by a resistant pathogen ΔV .

The data

In one of our previous studies, the impact of antibiotic use on the incidence of nosocomial MRSA infections was determined using a multivariate linear regression model.⁵ There was a positive impact for the use of second-generation cephalosporins (coeff.= 1.41, p = 0.023), third-generation cephalosporins (coeff.= 1.03, p = 0.051), fluoroquinolones (coeff.= 1.12, p = 0.01) and lincosamides (coeff.= 0.42, p = 0.05). Since logarithmically transformed variables were used in the regression, the dose-response rates ε equaled the resulting coefficients, which means that a one percent increase in third-generation cephalosporin use was followed by a 1.03 percent increase in the number of nosocomial MRSA infections. The linear assumptions made in the model made a constant dose-response relationship probable.⁹

Results

The study was conducted at University Medical Center Freiburg, a 1600 bed tertiary care teaching hospital. During the study period (January 2003 through October 2007), the mean monthly number of episodes of nosocomial infection was identified as being 2.69. Monthly antibiotic use is shown in Table 1. The probability of treatment-failure due to a resistant organism was calculated by using the monthly number of nosocomial MRSA infections in relation to the amount of antibiotics used. ($\sum \text{MRSA} / \sum \text{DDD}$; see Table 1).

Presuming that the additional cost of an MRSA-patient is significantly higher (8198€) than that of a non-MRSA patient,¹⁰ the calculations shown in Table 1 demonstrate the extent of the external cost of antibiotic consumption from promoting resistance.

(Insert Table 1 here)

Equally, equation (1) can be used to determine the positive effect of hand disinfection. Using existing data,⁵ we integrated the series of alcohol-based hand rub use into our multivariate model (coeff.= -5.37, $p < 0.001$). The negative coefficient estimated in the model shows the preventive impact of alcohol-based hand rub use on the incidence of MRSA. The results obtained from including alcohol-based hand rub use in equation (1) is shown in Table 1 and may be seen as the potential costs prevented by use of one litre of alcohol-based hand rub solution for hand disinfection. In other words, using only 3ml alcohol-based hand rub solution for hand disinfection, saves 0.18€ of the potential cost incurred by MRSA-related infections.

Discussion

As of yet, there are few studies demonstrating that use of antibiotics leads to indirect external costs by promoting resistance.^{7:8}

Although, the estimates presented here for the externality of antibiotic use are crude, they demonstrate that antibiotic consumption does from the perspective of a hospital, at least, substantially affect the cost of resistance. An externality of around 10 € per DDD is a small amount of money compared to the overall per diem cost of hospitalization, but is a significant amount compared to the direct cost of the antibiotic.

According to our calculations, a saving of approximately 14 € would be achieved by reducing use of third-generation cephalosporins by a single DDD. Increasing hospital-wide use of alcohol-based hand rub by one litre would give a saving of approximately 60 €. The emergence and spread of resistance in hospital settings is a multifactor process. Thus, prevention of AMR in the hospital can be only achieved by taking a multifactor approach in changing the major variables antibiotic use and infection control practice, especially hand hygiene. Both variables were tested in the multivariate time-series analysis.⁵

Demonstrating the net benefit of preventing AMR may lead to changes in prescribing behaviour and increase compliance with infection control practices.

Funding

Research on health and economic impacts of antibiotic resistance by K.K. and U.F. is currently supported by the European Commission (Project BURDEN, Project commissioned by DG SANCO, Grant Agreement N° 2005203; <http://www.eu-burden.info>).

Transparency declarations

No conflicts of interest.

Acknowledgement

We thank Deborah Lawrie-Blum for her help in preparing the manuscript.

Reference List

1. Levy SB. *The Antibiotic Paradox: How Miracle Drugs Destroying the Miracle*. New York, London: Plenum Press, 1992.
2. Frimodt-Moller N, Rosdahl N, Wegener HC. Microbiological resistance promoted by misuse of antibiotics: a public health concern. *Eur J Public Health* 1998;8(3):193-94.
3. Norrby SR, Nord CE, Finch R. Lack of development of new antimicrobial drugs: A potential serious threat to public health. *Lancet Infect Dis* 2005;5(2):115-19.
4. Aldeyab MA, Monnet DL, Lopez-Lozano JM et al. Modelling the impact of antibiotic use and infection control practices on the incidence of hospital-acquired methicillin-resistant *Staphylococcus aureus*: a time-series analysis. *J Antimicrob Chemother* 2008;62(3):593-600.
5. Kaier K, Hagist C, Frank U, Conrad A, Meyer E. Two time-series analyses of the impact of antibiotic consumption and alcohol-based hand disinfection on the incidences of nosocomial methicillin-resistant *Staphylococcus aureus* infection and *Clostridium difficile* infection. *Infect Control Hosp Epidemiol* 2009;30(4):346-53.
6. Vernaz N, Sax H, Pittet D, Bonnabry P, Schrenzel J, Harbarth S. Temporal effects of antibiotic use and hand rub consumption on the incidence of MRSA and *Clostridium difficile*. *J Antimicrob Chemother* 2008;62(3):601-7.
7. Elbasha EH. Deadweight loss of bacterial resistance due to overtreatment. *Health Econ* 2003;12(2):125-38.
8. Phelps CE. Bug/drug resistance. Sometimes less is more. *Med Care* 1989;27(2):194-203.
9. Kaier K, Frank U. An econometric view of the dynamic relationship between antibiotic consumption, hand disinfection and methicillin-resistant *Staphylococcus aureus*. *J Antimicrob Chemother* 2009;63(3):630-631.
10. Resch A, Wilke M, Fink C. The cost of resistance: incremental cost of methicillin-resistant *Staphylococcus aureus* (MRSA) in German hospitals. *Eur J Health Econ* 2009;doi: 10.1007/s10198-008-0132-3.

Table 1: Characteristics of the parameters used for the determination of the externality

q^a	Mean use of q^b	$R=$ $\frac{\sum \text{MRSA}}{\sum \text{DDD}}^c$	ε^d	ΔV^e	E^f
second-generation cephalosporins	6544	0.0004111	1.41	8 198 €	4.75 €
third-generation cephalosporins	1627	0.0016534	1.03	8 198 €	13.96 €
fluoroquinolones	2352	0.0011437	1.12	8 198 €	10.50 €
lincosamides	840	0.0032024	0.42	8 198 €	11.03 €
alcohol-based hand rub	1991	0.0013511	-5.37	8 198 €	-59.45 € ^g

^aUses of antibiotics and alcohol-based hand rub solution as included in the multivariate analysis.

^bMonthly amounts of antibiotic use (in DDD) and alcohol-based hand rub use (in litres) during the study period (01/2003 – 10/2007).

^cThe probability of the acquisition of a resistant infection.

^dDose-response rate of drug use – drug resistance as determined in the multivariate analysis.

^eThe additional costs of an Infection due to MRSA according to a recent study in 11 German hospitals.¹⁰

^fThe externality E of the use of one unit of q according to equation $E_q = \varepsilon_q R_q \Delta V$.

^gThe externality of alcohol-based hand rub use may be seen as potential costs prevented by one litre of alcohol-based hand rub use for hand disinfection.

Seit 2005 erschienene Beiträge

- No. 1 Christian **Hagist**/ Norbert **Klusen**/ Andreas **Plate**/ Bernd **Raffelhüschen**
Social Health Insurance – the major driver of unsustainable fiscal policy?
- No. 2 Stefan **Fetzer**/ Bernd **Raffelhüschen**/ Lara **Slawik**
Wie viel Gesundheit wollen wir uns eigentlich leisten?
- No. 3 Oliver **Ehrentraut**/Matthias **Heidler**/Bernd **Raffelhüschen**
En route to sustainability: history, status quo, and future reforms of the German public pension scheme?
- No. 4 Jasmin **Häcker**/ Bernd **Raffelhüschen**
Die Interne Rendite der Gesetzlichen Pflegeversicherung
- No. 5 Jasmin **Häcker**/ Bernd **Raffelhüschen**
Internal Rates of Return of the German Statutory Long-Term Care Insurance
(Englische Fassung von Diskussionsbeitrag No. 4)
- No. 6 Matthias **Heidler**/ Bernd **Raffelhüschen**
How risky is the German Pension System? The Volatility of the Internal Rates of Return
- No. 7 Laurence J. **Kotlikoff**/ Christian **Hagist**
Who's going broke? Comparing Growth in Healthcare Costs in Ten OECD Countries
- No. 8 Jasmin **Häcker**
Dynamisierung der Pflegeleistungen: Vergangenheit – Gegenwart – Zukunft
- No. 9 Dirk **Mevis**/ Olaf **Weddige**
Gefahr erkannt – Gefahr gebannt? Nachhaltigkeitsbilanz der 15. Legislaturperiode des deutschen Bundestages 2002-2005
- No. 10 Daniel **Besendorfer**/ Emily Phuong **Dang**/ Bernd **Raffelhüschen**
Die Schulden und Versorgungsverpflichtungen der Länder: Was ist und was kommt
- No. 11 Jasmin **Häcker**/ Bernd **Raffelhüschen**
Zukünftige Pflege ohne Familie: Konsequenzen des „Heimsog-Effekts“
- No. 12 Christian **Hagist**/ Bernd **Raffelhüschen**/ Olaf **Weddige**
Brandmelder der Zukunft – Die Generationenbilanz 2004
- No. 13 Matthias **Heidler**/ Arne **Leifels**/ Bernd **Raffelhüschen**
Heterogenous life expectancy, adverse selection, and retirement behavior
- No. 14 Pascal **Krimmer**/ Bernd **Raffelhüschen**
Grundsicherung in Deutschland - Analyse und Reformbedarf
- No. 15 Ulrich **Benz**/ Christian **Hagist**
Konjunktur und Generationenbilanz – eine Analyse anhand des HP-Filters
- No. 16 Jasmin **Häcker**/ Birgit **König**/ Bernd **Raffelhüschen**/ Matthias **Wernicke**/ Jürgen **Wettke**
Effizienzreserven in der stationären Pflege in Deutschland: Versuch einer Quantifizierung und Implikationen für die Reform der Gesetzlichen Pflegeversicherung
- No. 17 Christian **Hagist**/ Matthias **Heidler**/ Bernd **Raffelhüschen**/ Jörg **Schoder**
Brandmelder der Zukunft – Die Generationenbilanz Update 2007: Demografie trifft Konjunktur
- No. 18 Lukas **Mangelsdorff**
Die Geldsteuer: Vorschlag für eine radikal einfache Steuer
- No. 19 Jasmin **Häcker**/ Tobias **Hackmann**/ Stefan **Moog**
Demenzranke und Pflegebedürftige in der Sozialen Pflegeversicherung – Ein intertemporaler Kostenvergleich
- No. 20 Oliver **Ehrentraut**/ Matthias **Heidler**
Demografisches Risiko für die Staatsfinanzen? – Koordinierte Bevölkerungsvorsausberechnungen im Vergleich

- No. 21 Oliver **Ehrentraut**/ Matthias **Heidler**
Zur Nachhaltigkeit der GRV – Status quo, Potenziale und Risiken
- No. 22 Ulrich **Benz**/ Christian **Hagist**
Konjunktur und Generationenbilanz – eine Analyse anhand des HP-Filters
- No. 23 Ulrich **Benz**/ Christian **Hagist**
Technischer Anhang zu „Konjunktur und Generationenbilanz – eine Analyse anhand des HP-Filters“
- No. 24 Veronika **Deeg**/ Christian **Hagist**
The Fiscal Outlook in Austria – An Evaluation with Generational Accounts
- No. 25 Oliver **Ehrentraut**/ Bernd **Raffelhüschen**
Demografischer Wandel und Betriebsrenten – Zur Berücksichtigung der Langlebigkeit bei der Anpassung von Direktzusagen
- No. 26 Tobias **Hackmann**/ Stefan **Moog**
Älter gleich kränker? Auswirkungen des Zugewinns an Lebenserwartung auf die Pflegewahrscheinlichkeit
- No. 27 Klaus **Kaier**/ Christian **Hagist**/ Uwe **Frank**/ Elisabeth **Meyer**
Antimicrobial drug use, alcohol-based hand disinfection and the burden of methicillin-resistant Staphylococcus aureus – A time series approach at a German University Medical Center
- No. 28 Jasmin **Häcker**/ Tobias **Hackmann**/ Thorsten **Henne**
Sozialgesetzgebung und Beihilfeverordnungen: Ein Leistungsvergleich von Versicherten der Sozialen Pflegeversicherung und Beamten im Pflegefall
- No. 29 Stefan **Moog**
MacSim: Ein Simulationsmodell zur Analyse der gesamtwirtschaftlichen Auswirkungen der demografischen Entwicklung in Deutschland
- No. 30 Christian **Hagist**/ Stefan **Moog**/ Bernd **Raffelhüschen**
Ehrbarer Staat? Die Generationenbilanz – Update 2008: Migration und Nachhaltigkeit
- No. 31 Klaus **Kaier**/ Uwe **Frank**/ Christian **Hagist**/ Elisabeth **Meyer**
The impact of antimicrobial drug consumption and alcohol-based hand rub use on the emergence and spread of extended-spectrum β -lactamase (ESBL)-producing strains – A time series analysis
- No. 32 Friedrich **Fichtner**/ Christian **Hagist**
Oil and Intergenerational Redistribution – The case of Norway
- No. 33 Tobias **Hackmann**/ Stefan **Moog**
Pflege im Spannungsfeld von Angebot und Nachfrage
- No. 34 Christian **Hagist**/ Stefan **Moog**/ Bernd **Raffelhüschen** / Johannes **Vatter**
Ehrbare Staaten? Die Ergebnisse der Generationenbilanzierung im internationalen Vergleich
- No. 35 Christian **Hagist**/ Johannes **Vatter**
Measuring Fiscal Sustainability on the Municipal Level: A German Case Study
- No. 36 Uwe **Frank**/ Klaus **Kaier**
Dynamics between antibiotic drug use and resistance – An economic approach

Forschungszentrum Generationenverträge

Albert-Ludwigs-Universität Freiburg

Bertoldstraße 17

79098 Freiburg

Fon 0761 . 203 23 54

Fax 0761 . 203 22 90

www.generationenvertraege.de

info@generationenvertraege.de

ISSN 1862-913X