Impact of antimicrobial multidrug resistance on inpatient care cost: an evaluation of the evidence

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Keywords

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The alarmingly increasing antimicrobial resistance raises global concerns regarding the impact on patients with multidrug-resistant (MDR) infections. Important efforts have been made to study the clinical outcomes among patients infected with such pathogens, showing higher mortality and more frequent treatment failure among them compared with those infected with the susceptible isolates [1,2] . Apart from the worse clinical outcomes, MDR infections are expected to be more costly for healthcare systems than the susceptible ones, due to the higher length of stay (LOS) in the hospital associated with the infection [3,4] . A previous study has focused on the impact of common MDR Gram-negative (Gram[-]) bacilli, including the associated costs [5] . However, many new studies have been published since then and a cumulative collection and presentation of this important data has not yet been performed.

In this context, the authors aimed to systematically review and evaluate the available evidence in order to determine the impact of antimicrobial multidrug resistance on the inpatient care costs.

Methods

Literature search

The authors performed a systematic search in the PubMed and Scopus (Health Sciences and Life Sciences subject areas) databases in May 2012. The following search pattern was applied to all published articles: '(MDR or multidrug-resistant or extended-spectrum b-lactamase (ESBL) or carbapenem-resistant or imipenem-resistant or meropenem-resistant or MRSA) and (cost or economic or 'charges')'. In addition, the bibliographies of relevant studies were hand-searched in order to identify further studies potentially eligible for inclusion. Articles published in languages other than English, French, German, Spanish, Italian or Greek were not evaluated.

Study selection

Any article comparing the inpatient care costs of infection with MDR organisms (MDROs) with the costs of the non-MDRO of the same species was considered eligible for inclusion in this review. Studies evaluating only patients with colonization with MDROs were excluded. Multidrug resistance in Gram(-) bacteria was defined as resistance to three or more classes of antibiotics [6] . ESBL production in Enterobacteriaceae and carbapenem resistance (i.e., resistance to imipenem or meropenem) in Gram(-) nonfermentative bacilli or Enterobacteriaceae were types of antimicrobial resistance eligible for inclusion, as such pathogens are typically resistant to many classes of antibiotics. Finally, methicillin-resistant *Staphylococcus aureus* (MRSA) is, by definition, an MDR pathogen [7] ; thus, relevant studies on MRSA were also eligible for this review.

To clearly record the costs attributed to antimicrobial resistance, only studies providing the costs after the isolation of the pathogens

of interest for this review were considered eligible. Therefore, when studies reported on the costs of the total hospital LOS, including the period before the onset of infection, they were not included in the review. In addition, when the control group of a study comprised uninfected patients or patients with infections caused by pathogens with an indeterminate or ineligible antimicrobial resistance profile, this particular study was excluded. Finally, studies with a definition for MDR other than the aforementioned ones were not included.

Data extraction

Data were extracted regarding the characteristics of each study (first author, year, study design, period of the study and country) and the characteristics of the study population (number and main characteristics of the patients, type of infection and causative pathogens). Regarding the costs, a brief description of the type of costs recorded by each study was presented; the costs in each patient group, the attributable costs to antimicrobial resistance and the findings of the statistical analysis for the significance of the difference in costs, in case it was performed, were also extracted.

Definitions & outcomes

The definition of the inpatient care costs, given as costs, or as charges in a few studies, was based on the definitions given by the authors of the included studies.

The outcome of the review was the inpatient care costs attributable to antimicrobial resistance. For studies presenting the mean values of the inpatient care costs or hospital charges, the authors calculated the mean attributable costs as the difference in the mean costs between patients who had infections with an MDRO and patients with infections with a non-MDRO of the same species, using the relevant data from the original studies. If the costs or charges were presented in median values, the authors recorded the attributable costs given by each included study or the findings of the statistical analysis for the difference in costs or charges performed by each study. The eligible costs of a study were the total inpatient care costs. When the total costs were unavailable, the total hospital charges or specific costs, such as antibiotic costs, were used. All costs presented in Tables 1-3 are in US dollars (USD); in cases where the costs were given in another currency by the authors of a study [8-10] , a conversion to USD was performed according to the current exchange rate (as of when this was written).

Results

Through our literature search, 1450 articles were retrieved in the PubMed database, 2088 articles in Scopus and 18 articles by hand-searching, 24 of which were finally considered eligible for inclusion in the review [3,4,8-29] . The study selection process is depicted in Figure 1. Five studies were excluded as the provided costs referred to the total LOS in the hospital and not only to the period after the isolation of the studied pathogens [30-34] , and two additional studies were excluded because this was unclear [35,36] . One study was excluded because it provided relevant data only in the abstract, whereas the data were unavailable in the full text [37] .

The characteristics of the included studies are presented in the Tables 1-3. Seventeen studies had a retrospective cohort design [3,4,8,10-13,15,16,19,20,23,25-29] and seven studies had a retrospective case-control design [9,14,17,18,21,22,24] . Eight studies reported on ESBL-producing Enterobacteriaceae [4,8,9,12,18,22,28,29] , four studies [3,19,20,21] on carbapenem-resistant and MDR Gram(-) nonfermentative bacilli, and 12 studies reported on MRSA [10,11,13-17,23-27] . Relevant studies on carbapenem-resistant Enterobacteriaceae were not identified. All studies reported on hospitalized patients in acute care hospitals and in five of them, the infections were community-onset or community-acquired, according to the definitions provided in the studies [8,9,12,27,29] . Total inpatient care costs were provided by 17 studies [3,4,8,10,12-17,21-26,28] , hospital charges were provided by five studies [11,18-20,27] and only antibiotic costs by two studies [9,29] . Fifteen studies reported the mean values of the inpatient care costs or hospital charges [4,8,10,14,19-29] and the remaining nine reported the median values [3,9,11-13,15-18] .

Gram(-) nonfermentative bacilli

In the three studies reporting on carbapenem-resistant Gram(-) nonfermentative bacilli, the median costs were significantly higher for patients with carbapenem-resistant infections compared to those with carbapenem-susceptible infections of the same species in one study ($p < 0.01$) [3] , whereas the attributable mean hospital charges were US$58,457 and 85,299 in two other studies, respectively, which reported on infections or colonization with carbapenem-resistant organisms [19,20] . One study provided data on MDR *Acinetobacter baumannii* , where the attributable mean total costs were US$4484 [21] .

ESBL-producing Enterobacteriaceae

The attributable mean total costs varied from US$1,584 to 30,093 among four studies [4,8,22,28] . The median costs and median hospital charges of ESBL-positive infections were significantly higher than that of ESBL-negative infections of the same species in two studies (both $p < 0.001$) [12,18] . Regarding the two studies that provided data on the antibiotic costs only, the attributable mean cost was US$362 in one of these studies [29] , while in the other study, the median costs of the definitive treatment were only significantly higher among the subgroup of patients with bacteremia or respiratory tract infections due to ESBL(+) pathogens compared with those infected with ESBL(-) pathogens of the same species ($p = 0.002$) [9] .

Staphylococcus aureus

In the six studies that provided the mean total costs, the attributable costs varied from US$1,014 to US$40,090 [10,14,23-26] . The median total costs were significantly higher for patients infected with MRSA than those with methicillin-susceptible *S. aureus* infections in two studies ($p < 0.001$ and $p = 0.008$, respectively) [15,16] , and for patients who developed the MRSA infection while they were hospitalized in the intensive care unit (ICU) in another study compared with those who developed a methicillin-susceptible

S. aureus infection while hospitalized in the ICU ($p < 0.001$) .

Discussion

The inpatient care costs attributable to multidrug resistance are considerably high with over a 2.5-fold increase in one study [14] . With regards to hospital charges, a threefold increase among patients who had infections with MDROs was observed in one study as compared with those infected with non-MDRO of the same species [18] . The costs were significantly higher for MDR infections than non-MDR for the total study population in 17 out of 24 studies [3,4,8,11,12,14-16,18-23,25,28,29] and for subgroups of the study population in two studies (patients with respiratory tract or bloodstream infections in one study and patients who acquired the infection while they were hospitalized in the ICU in another one) [9,13] . On the contrary, the difference was not statistically significant in one study where the attributable costs had a negative value [27] . Of note, the large deviations in the absolute costs among the studies could be justified by the different cost of living among the countries included.

Meanwhile, certain explanations should be given in order to support the higher inpatient care costs of MDR infections. First, in 12 studies, all patients infected with MDR isolates had longer LOS in the hospital after the onset of infection compared with patients with infections due to the counterpart susceptible isolates [3,4,8,10-12,15,18,23-25,29] ; in one study, patients with MDR isolates who developed the infection while in the ICU [13] and in another one, those with bacteremia or respiratory tract infections caused by MDR isolates had longer LOS than patients with susceptible infections, as well [9] . Thus, higher costs for the healthcare system are expected due to lengthening LOS in the hospital.

Additional parameters that could affect the healthcare costs should be mentioned. Interestingly, 13 of the included studies showed that patients with MDR infections had a greater burden of comorbidity compared with those with the susceptible ones [3,4,8,10,11,13,15,16,18,20,23,28,29] . Furthermore, the longer LOS before infection in the patients with MDR infections (data provided by six studies) [3,4,13,20,22,23] , the fact that more patients with MDR infections were hospitalized in the ICU at the onset of infection (data provided by three studies) [3,20,23] and that these patients had more previous hospitalizations within the prior 3 or 12 months (data provided by two studies) [15,28] indicate that they could have more serious underlying comorbidity or a more complicated prior clinical course than the patients with the counterpart susceptible infections and therefore, higher costs ensure their management in the hospital. Finally, the higher use of antimicrobials within the prior months or the higher use of antimicrobials at admission or from admission to the onset of infection among the patients with MDR infections (according to data provided by six studies) [3,4,14,19,20,28] suggest a history of more frequent or difficult-to-treat infections in these patients and additionally, could justify the occurrence of MDRO isolates.

The above data imply that the higher inpatient care costs in patients with an MDRO could be attributed to the higher comorbidity and more complicated prior clinical course of these patients rather than the infection with an MDRO *per se* . The five studies that only examined patients with community-acquired, or even community-onset, infections could allow us to draw relevant conclusions without the potential influence of the above confounders [8,9,12,27,29] . Specifically, in studies [8,12,9,29] that reported the inpatient care and antibiotic costs, the costs were significantly higher among patients who had infections with ESBL(+) pathogens compared with those with ESBL(-) infections. Regarding the fifth study, the difference in hospital charges between the two compared groups was not statistically significant [27] . Even for community-onset infections, though, it cannot be excluded that patients with a resistant organism have greater underlying comorbidity than those with a susceptible organism.

Only two of the studies included in this review did not differentiate between infection and colonization with the studied pathogens [19,20] . Still, for the remaining studies, the differentiation between infection and colonization might not have been very accurate, due to their retrospective design. This again raises the question of whether it is the pathogen or the host that is associated with the worse outcome, in this case, the total inpatient care costs. This is an inherent limitation in studies addressing the impact of antimicrobial resistance, even in terms of mortality [38] . It should be mentioned, however, that colonization with an MDRO can be followed by infection in hospitalized patients during the course of their hospital stay. It is also plausible that isolates from cultures obtained at hospital admission may more frequently represent infection, unless these cultures were taken in the context of active surveillance; however, the latter practice was not reported in any of these studies. Thus, the five included studies that addressed the inpatient care costs in patients admitted in the hospital from the community may more accurately reflect the costs directly attributed to infection with an MDRO.

To our knowledge, this is the first review systematically recording the inpatient care costs attributable to antimicrobial multidrug resistance. Undoubtedly, this is an issue of great importance because apart from the worse clinical outcomes, MDR infections are responsible for higher costs for the healthcare systems. This implies that the establishment of appropriate infection control measures to control the spread of MDROs within a healthcare facility can be cost effective. This is particularly important for some low-income countries, where the problem of multidrug resistance is pronounced and the value of proper infection control might be underestimated.

The awareness of the costs associated with antimicrobial resistance may lead decision-makers and stakeholders into directing the available resources towards the reinforcement of the use of appropriate infection control measures in healthcare institutions.

Our study should be interpreted in light of certain limitations. First, the study design of all studies was retrospective; however, all of the studies directly assessed the issue of interest for this review, that is, the inpatient care costs or hospital charges with regard to multidrug resistance. Furthermore, different types of values (mean or median) regarding costs or charges were presented by the authors of the included studies and therefore, a meta-analysis of the data was not performed. Still, few studies provided the hospital charges instead of inpatient care costs, the latter being more representative for the scope of this review. In addition, much debate has been done with regard to the definition of multidrug resistance and therefore, studies may have been excluded due to the use of different definitions. We should also note that, despite excluding studies reporting on the cost during the whole LOS in the hospital, it

has been suggested that such an exclusion might not always be appropriate, if the LOS in the hospital prior to infection is the cause for the acquisition of the MDR infection and therefore, indirectly reflects the cost of the MDR infection [39] . However, such an adjustment could not be performed using the available data. Regarding the range of the literature included in the review, it should be mentioned that apart from the medical and health-economic journals of the PubMed and Scopus electronic databases, the pure economic literature was not searched. Last, in the four studies not presenting the costs in USD, a conversion to USD was performed using the current currency equivalent and not that of the time period of each study.

Expert commentary

An evaluation of the impact of antimicrobial multidrug resistance on inpatient care costs is now available. The costs were significantly higher for MDR infections than non-MDR infections for the total study population in 17 out of 24 studies, for patients with respiratory tract or bloodstream infections, and those who acquired the infection while they were hospitalized in the ICU in two other studies. On the contrary, the difference was not statistically significant in one study where the attributable costs had a negative value. The main finding of this review is that most studies agree that there is an association between MDR infections and increased inpatient care costs, across a range of organisms, types of infection, patient populations and healthcare systems.

Five-year view

The findings of this systematic review suggest that infection with an MDRO can have considerably high costs for a healthcare institution. On the basis of the available data however, we cannot directly assess whether this is associated with the risks attributed to the infection, or to the greater underlying comorbidity of the patients acquiring an MDRO. However, the above findings, along with the higher mortality associated with infection with an MDRO, emphasize the value of using the appropriate infection control measures to prevent the spread of MDROs in healthcare institutions.

Table 1. Studies on Gram(-) nonfermentative bacilli.

Study (year)	Study design; period, country	Patients (n); study population	Causative pathogen (s)	Description of cost	Cost		p-value for the difference in cost or charges	Attributable cost	Ref.
					Carbapenem-resistant or MDR	***Carbapenem-susceptible or non-MDR***			
Total inpatient care cost or hospital charges[dagger]									
Carbapenem resistance									
Lautenbach *et al.* (2010)	MC retrospective cohort; 2001-2006, USA	2542 (253 IRPA and 2289 ISPA); hospitalized patients with a culture positive for *Pseudomonas aeruginosa* (infection or colonization)	*P. aeruginosa*	Mean hospital charges	US$251,495	US$166,196	p < 0.001	US$85,299	[20]
Lautenbach *et al* . (2009)	MC retrospective cohort; 2001-2006, USA	386 (89 IRAB and 297 ISAB); hospitalized patients with a culture positive for *Acinetobacter baumannii* (infection or colonization)	*A. baumannii*	Mean hospital charges	US$334,516	US$276,059	p = 0.03	US$58,457	[19]
Lautenbach *et al* . (2006)	SC retrospective cohort; 1999-2000, USA	879 (142 IRPA and 737 ISPA); hospitalized patients with cultures positive for *P. aeruginosa* (infection)	*P. aeruginosa*	Median total cost (IQR)	US$81,330 (28,549-228,174)	US$48,381 (19,148-131,144)	p < 0.001	NR	[3]
MDR									

Lee *et al* . (2007)	SC retrospective case-control; 1996-2001, Taiwan	92; patients with nosocomial bacteremia	*A. baumannii*	Mean total cost ± SD	US$9349 ± 6323	US$4865 ± 4015	p = 0.001	US$4484	[21]

[dagger] All included studies report cost or charges after the infection or time of culture sampling.

IQR: Interquartile range; IRAB: Imipenem-resistant *Acinetobacter baumannii* ; IRPA: Imipenem-resistant *Pseudomonas aeruginosa* ; ISAB: Imipenem-susceptible *A. baumannii* ; ISPA: Imipenem-susceptible *P. aeruginosa* ; MC: Multicenter; MDR: Multidrug resistant; NR: Not reported; SC: Single center; SD: Standard deviation.

Table 2. Studies on extended-spectrum [beta]-lactamase-producing *Enterobacteriaceae* .

Study (year)	Study design; period, country	Patients (n); study population	Causative pathogen (s)	Description of cost	Cost		p-value for the difference in cost or charges	Attributable cost	Ref.
					ESBL positive	***ESBL negative***			
Total inpatient care cost or hospital charges [dagger]									
Hu *et al* . (2010)	MC retrospective cohort; 2006-2007, China	85 (32 ESBL[+] and 53 ESBL[-]); hospitalized patients with community-acquired IAIs	*E. coli, Klebsiella* spp.	Mean total cost	US$3604 (¥24,604)	US$2020 (¥13,788)	p < 0.001	US$1584 (¥10,816)	[8]
Tumbarello *et al* . (2010)	SC retrospective cohort; 2006, Italy	134 (37 ESBL[+] and 97 ESBL[-]); hospitalized patients with BSIs due to *Escherichia coli*	*E. coli*	Mean total cost ± SD	US$17,547 ± 20,480 (E13,709 ± 16,312)	US$11,115 ± 8392 (E8683 ± 6683)	p = 0.03	US$6432 (E5026)	[28]
Apisarnthanarak *et al* . (2008)	SC retrospective cohort; 2003-2007, Thailand	144 (36 ESBL[+] and 108 ESBL[-]); hospitalized patients with community-onset BSI	*E. coli, Klebsiella pneumoniae*	Median total cost (IQR)	US$615 (43-3173)	US$214 (53-1861)	p < 0.001	NR	[12]
Lee *et al* . (2006)	SC retrospective case-control (a 1:1 matching for the infecting pathogen and site of infection was performed) cohort; 2001-2004, USA	42; hospitalized patients with a positive for *E. coli* or *Klebsiella* spp. culture of a non-urinary tract specimen (infection)	*E. coli, Klebsiella* spp.	Mean total cost ± SD per patient	US$41,353 ± 39,607	US$24,902 ± 16,586	p = 0.04	US$16,451	[22]
Schwaber *et al* . (2006)	SC retrospective cohort; 2000-2003, Israel	198 (99 ESBL[+] and 99 ESBL[-]); hospitalized patients with bacteremia due to *Enterobacteriaceae*	*E. coli, Klebsiella* spp., *Proteus* spp.	Mean total cost per patient	US$46,970 (65,509 shekels)	US$16,877 (23,538 shekels)	p < 0.001	US$30,093 (41,971)	[4]
Lautenbach *et al*	SC retrospective case-control (a 2:1 matching for the infecting	99 (33 ESBL[+] and 66 ESBL[-]); hospitalized patients with cultures positive	*E. coli* , *Klebsiella*	Median hospital	US$66,590	US$22,231	p < 0.001	NR	[18]

. (2001)	pathogen and site of infection was performed); 1997-1998, USA	for *E. coli* or *Klebsiella pneumonia* (infection)	*pneumonia*	charges					
Antibiotic cost [dagger]									
Yang *et al* . (2010)	SC retrospective cohort; 2006-2008, Taiwan	58 (12 ESBL[+] and 46 ESBL[-]); hospitalized patients with community-onset bacteremic UTIs	*E. coli* , *K. pneumoniae*	Mean antibiotic cost ± SD	US$615 ± 424	US$253 ± 269	p = 0.01	US$362	[29]
Kola *et al* . (2007)	SC retrospective case-control; 2002-2004, Germany	69 (23 ESBL[+] and 46 ESBL [-]); hospitalized patients with community or nosocomially-acquired infections	*E. coli* , *K. pneumoniae*	Median total cost of definitive antibiotic therapy	US$408 or E325 (BSI, RTI)US$17 or E13 (UTI, wound infections)	US$74 or E59 (BSI, RTI)US$77 or E61 (UTI, wound infections)	p = 0.002 (BSI, RTI)p = 0.87 (UTI, wound infections)	NR	[9]

All costs presented are in US dollars; in cases where the costs were given in another currency by the authors of a study [8,9] , a conversion to US dollars was performed according to the current, as of when this was written, exchange rate.

[dagger] All included studies report on cost or charges after the infection or time of culture sampling.

+: Positive; -: Negative; BSI: Bloodstream infection; ESBL: Extended-spectrum b-lactamase; IAI: Intra-abdominal infection; IQR: Interquartile range; NR: Not reported; RTI: Respiratory tract infection; SC: Single center; SD: Standard deviation; UTI: Urinary tract infection.

Table 3. Studies on *Staphylococcus aureus* .

Study (year)	Study design; period, country	Patients (n); study population	Description of cost	Cost		p-value for the difference in cost or charges	Attributable cost	Ref.
				MRSA	*MSSA*			
Total inpatient care cost or hospital charges [dagger]								
Park *et al* . (2011)	SC retrospective propensity matched case-control; 2003-2008, Korea	106; hospitalized patients with bacteremia	Mean total cost ± SD	US$9370 ± 12,912	US$8356 ± 8959	p = 0.62	US$1014	[24]
Filice *et al* . (2010)	SC retrospective cohort; 2004-2006, USA	725 (335 MRSA and 390 MSSA); hospitalized patients with skin/soft tissue infection, UTI, pneumonia, bacteremia, other infections	Median total cost (IQR)	US$34,657 (11,517-98,287)	US$15,923 (5270-45,684)	p < 0.001	NR	[16]
Rubio-Terres *et al* . (2010)	MC retrospective cohort; 2005, Spain	366 (121 MRSA and 245 MSSA); hospitalized patients with bacteremia	Mean total cost per episode	US$14,093 (E11,045)	US$12,555 (E9839)	NR	US$1538 (1206)	[10]
		128 (55 MRSA						

Taneja *et al* . (2010)	SC retrospective cohort; 2005-2008, USA	and 73 MSSA); hospitalized patients with community-acquired pneumonia	Mean total hospital charges per admission ± SD	US$117,489 ± 132,164	US$135,784 ± 170,046	p = 0.51	-US$18,295	[27]
Anderson *et al* . (2009)	MC retrospective cohort; 1998-2003, USA	278 (150 MRSA and 128 MSSA); hospitalized patients with surgical site infections	Median hospital charges (IQR)	US$79,029 (38,113-127,846)	US$55,667 (22,201-86,757)	p = 0.01	Mean hospital charge attributable to methicillin resistance: US$24,113 (95% CI: 4521-43,704)	[11]
Ben-David *et al* . (2009)	SC retrospective cohort; 2000-2003, USA	182 (95 MRSA and 87 MSSA); hospitalized patients with bacteremia	Median total cost for those who acquired the infection while in the ICU and general unit, respectively	US$51,492 (ICU) US$23,690 (general unit)	US$17,603 (ICU) US$18,152 (general unit)	p < 0.001 (ICU) p = 0.3 (general unit)	NR	[13]
Cosgrove *et al* . (2005)	SC retrospective cohort; 1997-2000, USA	348 (96 MRSA and 252 MSSA); hospitalized patients with bacteremia	Median total cost (IQR)	US$14,655 (7768-27,998)	US$10,655 (5545-20,270)	p = 0.008	Average attributable hospital cost per patient: US$3836	[15]
Lodise *et al* . (2005)	SC retrospective cohort; 1999-2001, USA	353 (170 MRSA and 183 MSSA); hospitalized patients with bacteremia	Mean total cost	US$22,735	US$11,205	p < 0.001	US$11,530	[23]
Parvizi *et al* . (2010)	MC retrospective cohort; 1998-2008, USA	391 (231 MRSA and 160 MSSA); hospitalized patients with periprosthetic joint infection	Mean total cost ± SD per patient	US$107,264 ± 110,953	US$68,053 ± 50,354	p < 0.0001	US$39,211	[25]
Kopp *et al* . (2004)	SC retrospective case-control; 1999-2000, USA	72; hospitalized patients with bacteremia, pneumonia, skin infections, skeletal infections, UTI	Median total cost (IQR)	US$16,575 (7275-89,157)	US$12,862 (5292-36,471)	p = 0.1	NR	[17]
Rubin *et al* . (1999)	MC retrospective cohort; 1995, USA	NR; hospitalized patients with pneumonia, bacteremia, endocarditis, surgical site infections, osteomyelitis, septic arthritis	Mean total cost per patient	US$34,000	US$31,500	NR	US$2500	[26]
Boyce *et al* . (1981)	SC retrospective matched case-control; 1977-1978, USA	30; hospitalized patients with bacteremia and other infections	Mean total cost	US$64,370	US$24,280	p < 0.02	US$40,090	[14]

[dagger] All included studies report on cost or charges after the infection or time of culture sampling.

All costs presented are in US dollars; in cases where the costs were given in another currency by the authors of a study [8-10,28] , a conversion to US dollars was performed according to the current, as of when this was written, exchange rate.

ICU: Intensive care unit; IQR: Interquartile range; MC: Multicenter; MRSA: methicillin-resistant Staphylococcus aureus; MSSA: Methicillin-susceptible S. aureus; NR: Not reported; SC: Single center; SD: Standard deviation; UTI: Urinary tract infection.

Key issues

* It has been proven that patients with multidrug-resistant (MDR) infections experience worse clinical outcomes compared with those infected with the respective susceptible ones. MDR infections are expected to imply higher inpatient care costs as compared with non-MDR infections.

* We systematically review the available evidence in order to investigate the impact of antimicrobial multidrug resistance on inpatient care cost.

* The current review suggests that infection with an MDR organism (MDRO) can have considerably high costs for a healthcare institution.

* The available data, however, do not allow us to conclude whether the higher costs are associated with the risks attributed to the infection, or to the greater underlying comorbidity of the patients acquiring an MDRO.

* In conclusion, the worst clinical outcomes, along with the higher inpatient care costs observed among patients infected with an MDRO, establish the application of appropriate infection control measures in healthcare institutions as essential.

CAPTION(S):

Figure 1. Study selection process.

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Papers of special note have been highlighted as:

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** of considerable interest

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