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Research Article

Health-related quality of life of patients colonized or infected with multidrug-resistant organisms

Gesundheitsbezogene Lebensqualität von mit multiresistenten Bakterien kolonisierten oder infizierten Patienten

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Abstract

Aim: Due to their resistance against multiple antibiotics, multidrug-resistant bacteria (MDRO) impose higher costs upon health care providers and involve several risks for the health of patients. In the first place, the present paper aims to report on the applicability of a modified version of the German Short Form-36 (SF-36) Health Survey to address health-related quality of life (HRQoL) of inpatients colonized or infected with MDRO. Additionally, the study analyzes effects on HRQoL of affected patients.
Methods: A prospective intervention study was conducted to implement a multimodal hygiene program against MDRO in acute care hospitals within the Health Region Baltic Sea Coast in Germany. HRQoL was assessed at discharge from the attending ward and six months after, respectively. In addition, the SF-6D as a preference-based measure of health was calculated. In order to control for confounders, statistical matching was performed using the variables age, gender, hospital, hospital status (i.e., intervention vs. control group of the empirical study) and attending ward as matching criteria.
Results: Inpatients with MDRO (n=27) on average report lower scores for the majority of subscales. In addition, for these patients the component summary scores and the SF-6D are lower as well. With respect to follow-up examinations, the empirical data lead to no clear-cut impact on HRQoL for patients tested positive during their hospital stay.
Conclusion: The modified version of the German SF-36 has been shown to be a suitable instrument to measure HRQoL of patients colonized or infected with MDRO. In particular, our results indicate that MDRO impose a risk upon the health of colonized patients. As a consequence, effective prevention measures against MDRO may not only be beneficial for health care providers but for affected patients and for society as well.

Keywords: health-related quality of life, preference-based measure of health, economic evaluation, multidrug-resistant organism, methicillin-resistant Staphylococcus aureus

Zusammenfassung

Ziel: Aufgrund ihrer Unempfindlichkeit gegen verschiedene Antibiotika verursachen multiresistente Erreger (MRE) zusätzliche Kosten für Leistungserbringer und bewirken vielfältige Gesundheitsrisiken für Patienten. Die Studie untersucht zum einen die Anwendbarkeit einer modifizierten Version des deutschen Fragebogens zum Gesundheitszustand (SF-36) zur Messung der gesundheitsbezogenen Lebensqualität (health-related quality of life, HRQoL) von mit MRE kolonisierten oder infizierten stationären Patienten. Zum anderen wird der Einfluss multiresistenter Erreger auf die Lebensqualität betroffener Patienten analysiert.
Methoden: Im Rahmen einer prospektiven Interventionsstudie wurde ein multimodales Hygieneprogramm mit verschiedenen Präventionsmaßnahmen gegen MRE in Akutkrankenhäusern der Gesundheitsregion

Ostseeküste implementiert. Die gesundheitsbezogene Lebensqualität wurde bei Entlassung eines Patienten von einer teilnehmenden Station sowie sechs Monate nach Entlassung erfasst. Zusätzlich wurde der SF-6D als präferenzbasierter Nutzwert berechnet. Den MRE-positiven Patienten wurde durch statistisches Matching anhand der Variablen Alter, Geschlecht, Status des Krankenhauses (Interventions- oder Wartegruppe) sowie behandelnder Station eine geeignete Kontrollgruppe gegenübergestellt.

Ergebnisse: Im Durchschnitt weisen Patienten mit einer MRE-Kolonisation oder -Infektion (n=27) in der Mehrzahl der Dimensionen geringere Werte auf als Patienten ohne MRE. Auch die Werte der Summenskalen und des SF-6D fallen bei diesen Patienten niedriger aus. In Bezug auf die Entwicklung der gesundheitsbezogenen Lebensqualität nach Krankenhausaufenthalt zeigen sich keine eindeutigen Ergebnisse.

Schlussfolgerung: Die modifizierte Version des SF-36 stellt ein geeignetes Instrument zur Messung der gesundheitsbezogenen Lebensqualität von mit MRE kolonisierten oder infizierten Patienten dar. Ferner deuten die Ergebnisse darauf hin, dass multiresistente Erreger tatsächlich ein Gesundheitsrisiko für kolonisierte und infizierte Patienten bewirken. Infolgedessen profitieren nicht nur Leistungserbringer, sondern auch betroffene Patienten und die gesamte Gesellschaft von wirksamen Präventionsmaßnahmen.

Schlüsselwörter: gesundheitsbezogene Lebensqualität, präferenzbasierter Nutzwert, gesundheitsökonomische Evaluation, multiresistente Bakterien, Methicillin-resistenter Staphylococcus aureus

Introduction

Colonization with multidrug-resistant organisms (MDRO) involves several risks. An affected patient may develop an infection [1], [2], [3] or transmit the bacteria to other patients [4], [5], [6] or healthcare professionals, thus spreading the associated risks. Since these bacteria exhibit resistance against multiple antimicrobials, infections caused by MDRO will be more difficult to treat as there are fewer or even no effective antibiotics available [7]. For this reason, colonizations and, in particular, infections may cause additional costs for health care providers as well as severe health impairments and even death for affected patients [8]. A significant proportion of healthcare-associated infections is caused by the methicillin-resistant *Staphylococcus aureus* (MRSA), a Gram-positive bacterium exhibiting resistance not only against β-lactam antibiotics but also against other classes of antibiotics [9]. While over the last few years the proportion of MRSA to all *S. aureus* in most European countries has been stabilizing or even decreasing [9], hospitals and other healthcare facilities still face a serious problem as up to 24% of inpatients are colonized with MRSA [10]. In addition, the occurrence of other MDRO like vancomycin-resistant Enterococci (VRE) or multidrug-resistant Gram-negative bacteria (MRGN) including, e.g., multidrug-resistant *Acinetobacter baumanii* and extended-spectrum β-lactamases (ESBL) producing Enterobacteriaceae, has steadily increased [9], [11].

While the additional costs arising for hospitals due to MDRO and prevention measures against those pathogens have been studied extensively [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], only a few publications address the effects on health-related quality of life (HRQoL) of affected patients [8], [22], [23], [24]. Furthermore, these studies focus exclusively on the effects caused by MRSA colonizations and infections whereas the impact of other organisms like VRE and MRGN has been neglected in the literature.

The Short Form-36 (SF-36) Health Survey is one of the most widely used generic quality of life measures [25] which, e.g., was utilized by Jakob [23] in an investigation of HRQoL of cardiac surgery patients colonized or infected with MRSA. As demonstrated by Zwingmann et al. [26] and Mueller et al. [27], when applied to patients of hospitals, the original version of the German SF-36 questionnaire [28] may result in missing responses on some items due to formulations like “at work” and “at home”. To avoid this problem, Mueller et al. [29] introduced a modified version (SF-36m) of the questionnaire. Thus, the objective of our study is twofold: In the first place, we investigate the applicability of the SF-36m in addressing HRQoL of inpatients colonized or infected with MDRO. Furthermore, effects on HRQoL caused by MDRO are analyzed during hospitalization and via follow-up examinations six months after the patients' discharge, respectively.

Methods

Assessment of health-related quality of life during hospitalization

In 2011, the project HICARE (Health, Innovative Care And Regional Economy) was initiated in the Health Region Baltic Sea Coast in Germany in order to develop and evaluate interventions and innovations against MDRO [30]. One of the core elements of this project has been the HARMONIC (Harmonized Approach to avert Multidrug-resistant Organisms and Nosocomial Infections) study which was designed as a prospective intervention study that implements a hygiene program in acute care hospitals within the region. Among other things, the intervention comprised training of healthcare professionals in the prevention and handling of MDRO as well as recommendations on screening procedures. In order to detect MRSA, VRE and MRGN carriers as early as possible, screening upon admission was recommended for patients with pre-defined risk factors. Participating hospitals were either assigned to the intervention group where the hygiene program started right at the beginning of the study or to the control group where the intervention was implemented with a six months delay. Further details of the study are outlined by Gerlich et al. [31].

In order to account for the impact upon patients, HRQoL caused by MDRO is addressed as a nested study within the HARMONIC study by using the modified version (SF-36m) of the questionnaire introduced by Mueller et al. [29]. Since the average length of stay in German hospitals currently is about 7.3 days [32], we used the acute version of the questionnaire with a time horizon of seven days in order to gather information on HRQoL that does not relate to the time before hospitalization. Individuals participating in the HARMONIC study who have been tested for MDRO were asked to complete the questionnaire shortly before being discharged from the participating ward. In every participating hospital, data were obtained for three wards, i.e., an internal medicine ward, a surgical ward and an intensive care unit (ICU). Data collection on HRQoL took place from February 2013 to November 2014 [31].

Follow-up examination on health-related quality of life

Patients who were tested for MDRO during their hospital stay and agreed to participate in a follow-up examination received a set of survey documents by mail approximately six months after being discharged from the participating ward. More specifically, this set was sent by an independent trust agency in order to comply with data protection rules. It consisted of a cover letter, the acute version of the SF-36m, a second questionnaire on health care utilization during the period of six months after discharge as well as a reply-paid envelope addressed to the trust agency. Follow-up examinations on HRQoL were conducted from September 2013 to July 2015.

Preparation and evaluation of HRQoL data

The paper-based HRQoL questionnaires of the two measurement points were digitized by two persons. After checking for data out of range, the evaluation syntax for SF-36 questionnaires which was enclosed with the manual [28] was used to generate the data sets on HRQoL. These consisted of results on the eight subscales “physical functioning”, “role physical”, “role emotional”, “social functioning”, “bodily pain”, “vitality”, “general health” and “mental health” as well as the two component summary scores “physical summary score” (PSC) and “mental summary score” (MSC). While the eight dimensions are scored on a 0 (minimum) to 100 (maximum) scale, the two component summary scores are based on the US norm sample of 1990 (mean=50; standard deviation=10) with higher values indicating a better HRQoL [28].

While the values of the eight dimensions and the component summary scores reflect the impact on health-related quality of life, it is important to observe that they do not represent individual preferences for health. In particular, the values derived from the SF-36 cannot be used directly in cost-utility analyses [33], [34]. Therefore, we used the SF-6D (scored on a 0.29 to 1 (perfect health) scale [25]) developed by Brazier et al. [33] in order to calculate a preference-based measure of health. After fulfilling the license application form [35], the program to calculate the SF-6D from an existing SF-36 data set along with a license was obtained from the University of Sheffield.

After calculating the values described above, some data sets had to be eliminated. More specifically, this concerns data sets that could not be assigned to any study participant as well as data sets with incomplete information on at least one of the eight subscales or the SF-6D. For unknown reasons, two patients completed two questionnaires on HRQoL while being hospitalized. In these cases, one of the two electronic data sets was randomly selected for deletion.

Since the objective of the follow-up examination was to assess the change in HRQoL six months after discharge from the hospital, for this evaluation we deleted all data sets of patients for whom we did not have complete information on the questionnaire both at discharge from the participating ward *and* during follow-up examination.

Statistical analysis

Patients with a positive screening result or an incidental finding during hospitalization were taken to be colonized or infected with MDRO. In order to control for confounders, we used statistical matching to capture the effect caused by MDRO on HRQoL. More specifically, every patient colonized or infected with MDRO was matched to a patient without any multi-resistant patho-

gen. Since these variables can be expected to influence both colonization status and HRQoL, matching was performed using the covariates gender and age (±5 years). As the principal diagnosis and other predictors of the underlying health status were not available for all study participants, we used the attending hospital ward (i.e., internal medicine, surgical or ICU) as a covariate to account for differences in the underlying disease. In essence, this implies the allocation of a patient to a hospital ward to be influenced by her disease but not by her MDRO status. Moreover, both the hospital and hospital status (i.e., intervention group vs. control group of the HARMONIC study) were used as further matching criteria to account for possible differences in hygienic measures which could either affect the carriership of patients or their HRQoL. Data sets which did not contain full information on the matching criteria were deleted for evaluation purposes.

Based on the search algorithm described by Smith [36] and Bacher [37], data files containing patients with and without MDRO, respectively, were sorted randomly. Next, statistical twins among the subgroup of patients without MDRO matching the criteria described above were identified for every MDRO patient beginning with the first one in the randomly sorted data file. If more than one possible control was available within the range of age, the one with the minimum distance in age was chosen. Matching without replacement was performed, i.e., an individual already selected as control could not be used again for another MDRO patient.

In order to test for normal distribution, we performed Kolmogorov-Smirnov tests on the data sets. As the values for some of the dimensions exhibit statistically significant deviations from the normal distribution, Wilcoxon signed rank tests were used in order to test for statistical differences in HRQoL and the preference-based measure SF-6D between the groups. A level of ≤ 0.05 was considered statistically significant while the levels of ≤ 0.01 and ≤ 0.001 were considered highly and extremely significant, respectively. IBM SPSS Statistics version 20 was used for the statistical analysis of the data.

Results

Study population and applicability of the instrument

During the period of the HARMONIC study we received 731 SF-36m questionnaires. Out of these, 693 could be assigned to individuals by the workflow-oriented documentation system. After deleting two data sets of patients who completed the SF-36m twice and data sets with incomplete information on either HRQoL or at least one of the matching criteria, 475 (64.98%) data sets of participating individuals remained for evaluation purposes.

At least one MDRO was found via admission screening or as an incidental finding during hospital stay for 32 patients (6.74%), with three patients being carriers of two and one even of three types of multidrug-resistant bacteria. More specifically, eighteen patients (3.79%) were found to be colonized with MRSA, five (1.05%) with VRE and six (1.26%) with ESBL while seven (1.47%) were colonized with bacteria resistant to three classes of antibiotics (3MRGN) and one patient (0.21%) with a bacterium even resistant to four classes of antibiotics (4MRGN). Table 1 displays the descriptive statistics of the pre-matched study population. Clearly, patients with MDRO are more likely to be male and older than patients without MDRO. Furthermore, patients with a multi-resistant pathogen are more likely to be treated on an intensive care unit.

Table 1: Descriptive statistics of the pre-matched sample
(Source: own)

	Patients without MDRO (N=443)	Patients with MDRO (N=32)
gender	248 men (55.98%)	22 men (68.75%)
mean age (SD)	62.51 (15.57) years	69.09 (13.37) years
attending ward		
internal medicine ward	188 (42.44%)	10 (31.25%)
surgical ward	179 (40.41%)	11 (34.38%)
ICU	76 (17.16%)	11 (34.38%)

SD = standard deviation; ICU = intensive care unit

In addition, 707 survey sets were sent to individuals who had agreed to participate in a follow-up examination. Overall, we received 369 SF-36m-questionnaires, amounting to a response rate of 52.19%. Again, data sets have been deleted that either could not be assigned to patients or relate to patients for whom we received incomplete information on their HRQoL. Thus, accounting for both measurement points, i.e., the discharge from the participating hospital ward *and* the follow-up examination, we obtained 153 data sets in total for evaluation purposes. Out of these, twelve (7.84%) relate to patients with MDRO during their hospital stay, with six being colonized with MRSA and six being colonized with other types of MDRO.

The number of evaluable questionnaires fulfilled by patients colonized or infected with MDRO indicates that the SF-36m is a suitable measure to address HRQoL of inpatients both during hospitalization and follow-up examination.

Health-related quality of life during hospitalization

For twenty-seven of the patients with MDRO, we were able to find a negative control, i.e. a patient without MDRO, applying the matching criteria described above. As Table 2 indicates, patients being colonized with at least one MDRO on average report lower scores for the majority of the subscales as measured by the SF-36m, the only exception being the *general health* dimension.

Table 2: HRQoL and SF-6D for patients with and without MDRO
(Source: own)

	Patients with MDRO N=27		Patients without MDRO N=27		p-value
	mean (SD)	median	mean (SD)	median	
physical functioning	21.89 (27.17)	10.00	35.00 (27.17)	30.00	0.037*
role physical	12.04 (30.52)	0.00	21.30 (39.65)	0.00	0.375
bodily pain	43.48 (40.72)	22.00	46.44 (29.17)	41.00	0.715
general health	53.96 (14.76)	50.00	48.74 (20.07)	47.00	0.484
vitality	34.44 (24.90)	25.00	38.15 (23.62)	35.00	0.674
social functioning	56.94 (32.77)	62.50	60.65 (32.84)	62.50	0.701
role emotional	41.98 (49.43)	0.00	62.96 (45.60)	100.00	0.071
mental health	48.81 (30.74)	48.00	61.78 (28.38)	68.00	0.150
PSC	29.84 (7.59)	27.08	30.21 (9.12)	29.66	0.665
MSC	41.89 (17.19)	37.23	47.27 (14.85)	49.34	0.259
SF-6D	0.544 (0.176)	0.558	0.586 (0.128)	0.579	0.212

SD = standard deviation; * statistically significant on the 5%-level

Table 3: HRQoL and SF-6D for patients with and without MRSA
(Source: own)

	Patients with MRSA N=16		Patients without MRSA[1] N=16		p-value
	mean (SD)	median	mean (SD)	median	
physical functioning	22.57 (25.27)	12.50	37.81 (28.81)	35.00	0.093
role physical	0.00 (0.00)	0.00	23.44 (40.28)	0.00	0.039*
bodily pain	46.75 (39.13)	36.50	50.38 (30.62)	46.00	0.683
general health	54.94 (13.98)	47.50	48.38 (22.97)	48.50	0.507
vitality	35.94 (23.75)	32.50	35.94 (20.51)	32.50	0.979
social functioning	58.59 (30.86)	62.50	60.94 (35.90)	68.75	0.789
role emotional	39.58 (49.02)	0.00	62.50 (46.94)	100.00	0.177
mental health	50.75 (29.38)	58.00	61.00 (27.46)	66.00	0.320
PSC	29.19 (7.28)	27.43	31.53 (10.18)	31.14	0.326
MSC	42.69 (16.95)	41.55	46.27 (14.76)	48.10	0.501
SF-6D	0.544 (0.144)	0.543	0.594 (0.147)	0.616	0.379

SD = standard deviation; * statistically significant on the 5%-level

[1]The group of patients without MRSA only includes patients who were also tested negative for other MDRO pathogens.

More specifically, the impairment in the *physical functioning* subscale is statistically significant. In addition, for patients with MDRO during hospitalization, the two component summary scores PSC and MSC as well as the preference-based measure of health, the SF-6D, turn out to be lower as well.

While Table 2 contains the results on HRQoL of patients with *any* MDRO, Table 3 depicts the results for patients with MRSA in comparison to the controls as matched on the criteria indicated above. Even though the focus has been narrowed, the results turn out to be broadly similar to the ones obtained for the general case of MDRO. More specifically, for patients with MRSA, HRQoL is reduced in six subscales, with a statistically significant impairment in the *role physical* dimension. However, while the vitality of patients does not seem to be affected, patients with

MRSA on average reported higher HRQoL in the *general health* dimension. On the other hand, both summary scores PSC and MSC as well as the preference-based measure of health as given by the SF-6D on average turn out to be lower for patients with MRSA.

Follow-up examination on health-related quality of life

On average, the 153 patients with complete data sets for both surveys on HRQoL filled in the second SF-36m questionnaire 206.4 days (SD=26.17 days) after the first one and after being discharged from the participating hospital ward, respectively. As Table 4 indicates, for the 141 patients without MDRO during their hospital stay, HRQoL on average increased in almost every dimension. Correspondingly, both the physical and mental component summary scores have risen as well. For that reason, there was also a statistically significant improvement in the SF-6D. In contrast, for patients with MDRO during hospitalization, the results for the change in HRQoL in the post-discharge period are less clear-cut. While the scores in the subscales *physical functioning*, *role physical*, *role emotional* and *social functioning* increased on average, the scores in the other dimensions decreased. As a result, the MSC slightly went down whereas the PSC shows a slight increase between the two measuring points. Referring to the *general health* subscale, it should be noted that both subgroups reported statistically significant lower values at the post-discharge measuring point.

Discussion

Our results indicate that the modified version of the SF-36 Health Survey is a suitable measure to address health-related quality of life of inpatients affected by multidrug-resistant bacteria. Furthermore, the results suggest that the impact of MDRO upon individual health is negative since HRQoL is lower for hospitalized MDRO carriers in almost every dimension. In Germany, regulatory stipulations for the handling of different MDRO include the recommendation that patients with MRSA or MRGN should be separated from other patients [38], [39]. As a consequence, impairments in the *social functioning* dimension reflecting limitations in social interactions could be expected. Although this conjecture is not confirmed by our data, patients with MDRO in general and with MRSA in particular have been shown to suffer from negative effects in the psychological dimension of health as reflected by the *role emotional* and *mental health* subscales. Moreover, since these patients also reported negative impacts on the *physical functioning* and the *role physical* subscales, there seem to be some physical limitations as well.

Given that an infection with MDRO is known to affect health-related quality of life rather severely, at first sight it may be surprising that in our sample of patients, with the exception of the *physical functioning* subscale, the effect of MDRO turns out to be too weak to be statistically significant. This can be explained as follows. First, we cannot distinguish whether a patient with MDRO is only colonized or suffers from an infection. Apart from a possible harm due to isolation [40] and decolonization therapy, a mere colonization is expected to have no further negative impact on health-related quality of life. Second, as noted above, the subsample of patients with MDRO refers to patients who have been tested positive for MDRO. In view of the low prevalence of MDRO even among patients with risk factors, the predictive value of a positive test result will be less than 0.5 despite high values for sensitivity and specificity. Therefore, our subsample of patients tested positive very likely includes only a share of patients with MDRO and, among these, the subset of patients with an MDRO infection will be rather small.

The purpose of the follow-up examination has been to evaluate long-term effects of MDRO colonizations and infections on HRQoL. However, since the values in some of the subscales increased while the values of others decreased, our investigation failed to produce unambiguous results on how HRQoL of patients tested positive for MDRO changed in the post-discharge period. As the preference-based measure of health, the SF-6D, slightly increased on average, this may indicate that on the whole there is a post-discharge improvement in health not only for MDRO negative patients but also for those patients colonized or infected with multidrug-resistant bacteria.

Nevertheless, the results of the follow-up examination on HRQoL might be biased due to the MDRO status at the second measuring point or to a disease that was either not present or not known at the time of discharge. To avoid such a bias, the above mentioned questionnaire on post-discharge health care utilization also contained questions on actual MDRO status and on newly emerged diseases, respectively. First, participants were asked whether they were currently colonized with any MDRO. More specifically, 145 participants responded to this question. Out of those 134 who had been tested negative for MDRO during hospitalization, nobody stated to be a MDRO carrier within the post-discharge period while 32 (23.88%) did not know. Out of those 11 tested positive for MDRO during hospital stay, one participant (9.09%) was still colonized while 7 (63.63%) were no MDRO carriers any more. Finally, 3 patients (27.27%) did not know their actual MDRO status. Moreover, individuals were asked whether a disease has been newly diagnosed in the last six months. If so, participants were then requested to indicate how much this has affected their physical and emotional well-being. While 148 individuals responded to the former question, only 20 (13.5%) of the participants stated that a disease was newly diagnosed in the post-discharge period. More precisely, since the latter patients mostly indicated that their emotional and physical wellbeing due to this disease either was not affected at all or just a bit, we conclude that the results of the follow-up examination on HRQoL are not biased by unknown diseases.

Table 4: HRQoL at hospital discharge and follow-up (FU) for patients with and without MDRO during hospital stay
(Source: own)

	Patients with MDRO (hospital) N=12		Patients with MDRO (FU) N=12		p-value	Patients without MDRO (hospital) N=141		Patients without MDRO (FU) N=141		p-value
	mean (SD)	median	mean (SD)	median		mean (SD)	median	mean (SD)	median	
physical functioning	41.57 (26.84)	42.50	42.08 (28.32)	32.50	0.859	46.19 (28.78)	40.00	58.05 (31.05)	60.00	<0.001***
role physical	12.50 (31.08)	0.00	54.17 (46.26)	62.50	0.068	28.72 (40.74)	0.00	47.52 (43.95)	50.00	<0.001***
bodily pain	58.25 (38.18)	46.00	55.50 (29.81)	41.50	0.635	51.89 (32.46)	41.00	61.72 (28.75)	62.00	0.001***
general health	58.67 (16.26)	58.50	41.69 (16.64)	37.00	0.037*	57.05 (18.13)	55.00	52.81 (22.49)	52.00	0.006**
vitality	47.92 (20.72)	50.00	44.44 (13.34)	47.50	0.689	46.04 (23.21)	45.00	52.38 (21.33)	50.00	0.004**
social functioning	64.58 (34.47)	68.75	76.04 (21.62)	75.00	0.283	69.59 (28.32)	75.00	78.37 (23.81)	87.50	0.002**
role emotional	69.44 (45.97)	100.00	72.22 (39.78)	100.00	0.832	64.07 (45.26)	100.00	66.67 (44.19)	100.00	0.584
mental health	68.83 (23.05)	68.00	65.75 (14.41)	66.50	0.959	65.70 (22.35)	72.00	70.85 (18.59)	76.00	0.016*
PSC	32.46 (6.92)	31.97	34.30 (9.59)	34.81	0.530	34.35 (10.40)	34.09	38.58 (12.30)	39.42	<0.001***
MSC	50.16 (14.04)	51.32	49.89 (7.69)	50.16	0.814	48.75 (13.30)	51.67	50.00 (11.18)	52.24	0.478
SF-6D	0.639 (0.163)	0.6325	0.655 (0.114)	0.658	0.583	0.627 (0.141)	0.600	0.689 (0.141)	0.675	<0.001***

SD = standard deviation; * statistically significant on the 5%-level, ** statistically significant on the 1%-level, *** statistically significant on the level 0.1%-level

Another limitation of our study relates to the preference-based measure of health. More specifically, the health states underlying the SF-6D were valued by a representative sample of the UK general population [33]. In view of the possibility that the preferences of the German and the British population may not necessarily coincide, the results should be interpreted with caution.

Since the objective of this study was to address the effect of MDRO on health-related quality of life, an ideal setting would involve the comparison of HRQoL of individuals differing only with respect to the variable of interest, i.e., MDRO colonization. In order to control for the influence of other variables, statistical matching was performed relying on the criteria age, gender and the attending hospital ward. Nevertheless, due to the design and the implementation of the empirical study, it has not been feasible to control for other relevant variables representing potentially important confounders. More specifically, due to missing information on the main diagnosis for a sizeable proportion of the participating individuals, the underlying disease could not be used as a matching criterion even though it may well have a significant impact on HRQoL. Furthermore, since we lacked information on the quantity and severity of secondary diagnoses, matching on these variables could not be performed either.

The low prevalence of MDRO within the inpatient population as well as the rather small number of individuals participating in both surveys on HRQoL involves another limitation of our study. In order to obtain a sufficiently large number of participating individuals, the bulk of the statistical analysis has been performed for all individuals who were tested positive for *any* MDRO and MRSA, respectively. Instead, with considerably larger patient samples, a more targeted approach would be to separate the study participants tested positive for MRDO in individual groups, e.g., leading to subsets of patients tested positive for VRE and MRGN. As it is, the pooling of all MDRO may cause a bias in the results on HRQoL if the type of MDRO is important for the size of the effect upon HRQoL.

Despite these limitations, the present paper represents the first study examining the effect of MDRO on inpatients' HRQoL followed by another examination which is carried out post-discharge. In contrast, the literature up to now has only addressed health effects caused by MRSA while studies on other MDROs' effect on HRQoL are not available. For example, also relying on appropriate matching, Pada et al. [8] examined the effect caused by MRSA infections on HRQoL. Using the EuroQol-5D (EQ-5D) summary index, the authors found a strong negative impact of MRSA on HRQoL. While the fact that the influence of MRSA is more pronounced than in our study can be explained by the exclusive focus on infections, it is important to note that there is no consideration of HRQoL after discharge [8].

Another study by Laudermilch et al. [22] investigated the effect of MRSA infections on functional scores of patients who underwent revision of total knee arthroplasty two years after hospital discharge by using, among other measures, the SF-36 to evaluate the effect on HRQoL. The results of the two component summary scores correspond closely with the findings of our follow-up examination as Laudermilch et al. reported the PSC and the MSC to be 37.9 (SD=16.7) and 50.5 (SD=15.6), respectively. On the other hand, since the results of our follow-up examination also include data of patients who have been tested positive for MDRO other than MRSA, our analysis is more general.

Finally, the retrospective study by Jakob [23], which was also carried out in Germany, investigated HRQoL as measured by the SF-36 of 18 cardiac surgery patients colonized or infected with MRSA in comparison with 18 matched controls. Matching was performed with a number of criteria, among them age, sex, duration of surgery, length of hospital stay, and duration of postoperative hemorrhage. The survey was conducted three to five years after discharge via telephone interview. In seven dimensions, Jakob found statistically significant impairments due to MRSA while only the effect relating to the *bodily pain* subscale failed to be significant. Nevertheless, given the design of the study and its focus on MRSA, the results offer only limited guidance on the impact of MDRO on HRQoL in general.

Conclusions

The present paper represents the first study to address effects on health-related quality of life during hospitalization caused by multidrug-resistant bacteria which is not confined to the methicillin-resistant *Staphylococcus aureus*. Our results indicate that inpatients do indeed suffer from MDRO since they report lower scores in almost all dimensions of HRQoL as measured by the modified version of the SF-36. Furthermore, our analysis breaks new ground by also evaluating the development of post-discharge HRQoL of patients who have been tested for MDRO. Overall, however, the empirical data lead to no clear-cut impact on HRQoL with respect to follow-up examinations for patients tested positive during their hospital stay as the scores in some dimensions increased on average, while the scores in others decreased. Clearly, further research on this topic is necessary as our study is limited by a rather small number of MDRO positive patients participating in both surveys. Turning to treatment within hospitals, it is well-known that MDRO impose a financial burden on health care providers. Our results indicate that health-related quality of life of patients is also at risk. As a consequence, effective prevention measures against multidrug-resistant bacteria may not only improve health care provision but also be beneficial to society.

Notes

Competing interests

The authors declare that they have no competing interests.

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Human rights and informed consent

The study was approved by the local Ethical Committees and informed consent was obtained from all individual participants included in the study. For further details see Gerlich et al. [31].

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