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### **Citation**

Wijnakker, R., Lambregts, M. M. C., Rump, B., Veldkamp, K. E., Reis, R., Visser, L. G., & Boer, M. G. J. de. (2020). Limited multi-drug resistant organism related stigma in carriers exposed to isolation precautions: an exploratory quantitative questionnaire study. *Journal Of Hospital Infection*, 106(1), 126-133. doi:10.1016/j.jhin.2020.06.034

Version: Publisher's Version

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**Note:** To cite this publication please use the final published version (if applicable).



# Limited multi-drug resistant organism related stigma in carriers exposed to isolation precautions: an exploratory quantitative questionnaire study

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## ARTICLE INFO

### Article history:

Received 22 March 2020

Accepted 29 June 2020

Available online 3 July 2020

### Keywords:

MDRO

Stigma

Mental health

Isolation precautions

Quantitative study



## SUMMARY

**Background:** Isolation precautions are applied to control the risk of transmission of multi-drug resistant organisms (MDROs). These precautions have been associated with adverse effects, such as anxiety and depression. This study aimed to quantify stigma among MDRO carriers and its association with perceived mental health and experienced quality of care.

**Methods:** A quantitative questionnaire study was performed in MDRO carriers exposed to  $\geq 3$  days of isolation precautions during hospitalization. Items derived from the Consumer Quality Index questionnaire (CQI) were used to assess perception of care. Stigma scores were calculated using the recently modified Berger Stigma Scale for meticillin-resistant *Staphylococcus aureus* (MRSA). Mental health was measured with the RAND Mental Health Inventory. The Spearman rank correlation test was used to assess the association between stigma score and RAND mental health score.

**Findings:** Of the 41 included carriers, 31 (75.6%) completed both questionnaires. The experienced quality of care was 'good' according to CQI score. Twenty-four percent reported not to have received proper explanation about MDRO carriership from healthcare workers (HCWs). MDRO-associated stigma was reported in 1/31 (3.2%). Poor mental health was self-reported in 3/31 (9.7%). There was no correlation between stigma score and RAND mental health score (Spearman correlation coefficient: 0.347).

**Conclusions:** In this study, MDRO carriers exposed to  $\geq 3$  days of isolation precautions did not report stigma. This contrasts with a recent study that investigated MRSA-associated stigma and may be explained by contact plus airborne isolation protocols in MRSA

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compared with contact isolation alone in most other MDROs. Also, the psychological impact may be of a different magnitude due to as yet unknown reasons.

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## Introduction

In 2014, the WHO stated that antimicrobial resistance (AMR) is a worldwide problem requiring urgent action [1]. Increasing levels of AMR are a threat to global health and hence controlling the spread of MDROs is of major public interest. Isolation precautions are a cornerstone in preventing MDRO transmission [2–5]. For standard contact precautions in our hospital the patient is placed in a single-bed room and healthcare workers (HCWs) wear gowns and gloves during contact. For contact plus airborne isolation, HCWs wear gowns, gloves and masks, and single-patient rooms equipped with special air handling and ventilation capacity are used [2].

Many adverse impacts of isolation have been described in the literature. Patients may be at increased risk of preventable adverse events such as pressure ulcers [3,4]; this may be one impact of HCWs entering the rooms of isolated patients less frequently than the rooms of patients without isolation precautions [5]. Isolation precautions can increase hospital length of stay, because of delays in undertaking diagnostic or surgical procedures, or transferring patients to other institutions [3–5]. Also, patients in isolation rooms may experience stronger feelings of anxiety, depression and decreased wellbeing compared with hospitalized patients without isolation [4–13]. HCWs are perceived as uncaring and carriers are more likely to express dissatisfaction with their care. This can be stigmatizing for the social interaction within healthcare [14–19].

MDRO-related stigma is important because it can contribute to the burden of illness and may influence the effectiveness of control of transmission. Moreover, MDRO carriers who experience stigma may be less likely to report their colonization status in the future. A stigma is defined as “a social process, experienced or anticipated, characterized by exclusion, rejection, blame or devaluation that result from experience, perception or reasonable anticipation of an adverse social judgement about a person or a group” [20]. Stigma has been evaluated in relation to various infectious conditions such as HIV, leprosy, epilepsy, and most recently meticillin-resistant *Staphylococcus aureus* (MRSA) [21]. Most instruments to measure the intensity and quality of stigmata are condition-specific qualitative measures [22].

This study aims to quantify the stigmatization perceived by patients who isolated during their hospitalization due to MDRO colonization. A secondary aim was to correlate the stigma score with perceived mental health.

## Methods

### Setting and study population

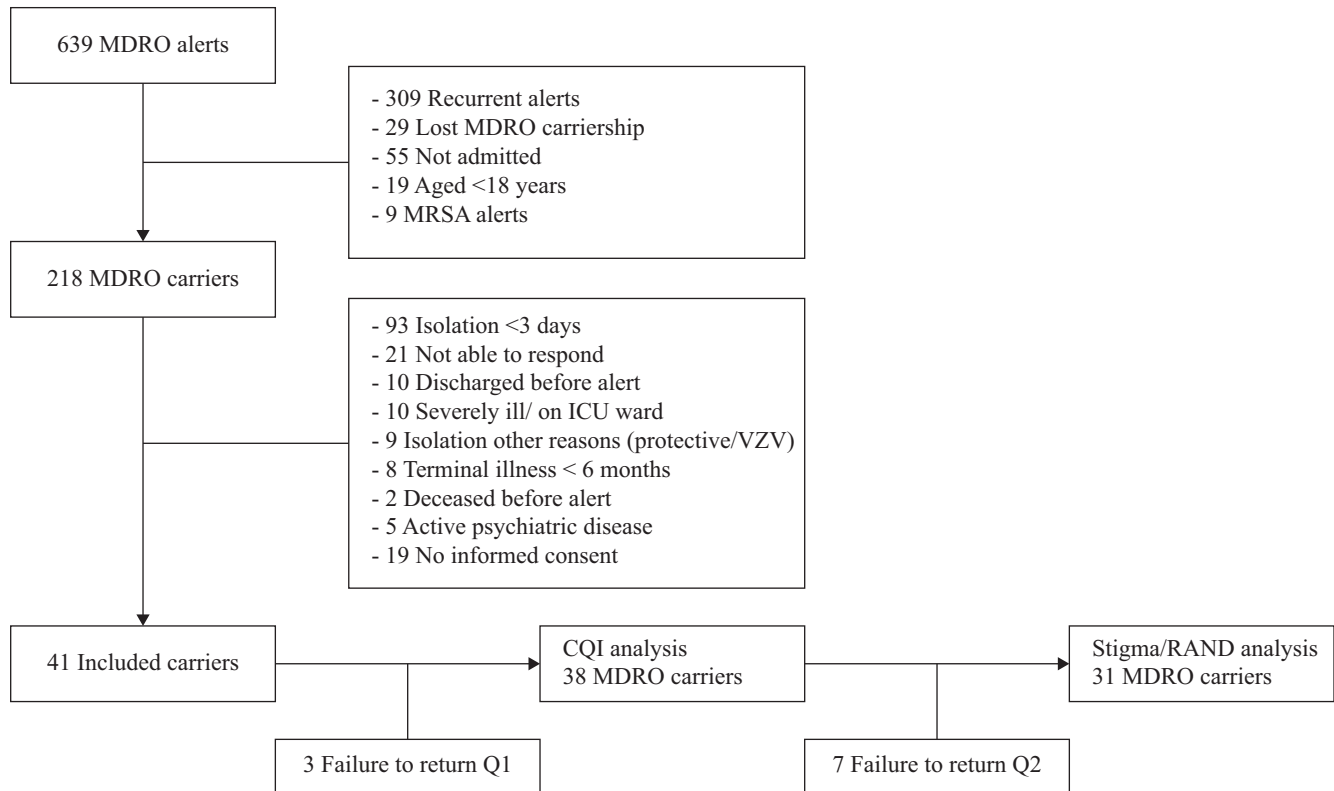
Between September 2018 and February 2019, a cross-sectional, questionnaire study was performed in a tertiary care and teaching centre in the Netherlands. Potential participants in the study were identified by the Infection Prevention Department automatically received an e-mail alert

**Table 1**  
Definitions of multidrug-resistant organisms (MDRO) used in this study [2]

Definition of highly resistant Enterobacterales							
Enterobacterales	ESBL	Quinolones	AG	Carbapenems	Co-trimoxazole		
<i>Escherichia coli</i>	A	B <sup>a</sup>	B <sup>a</sup>	A	N/A		
<i>Klebsiella</i> spp.	A	B <sup>a</sup>	B <sup>a</sup>	A	N/A		
Other	A	B <sup>a</sup>	B <sup>a</sup>	A	B <sup>a</sup>		
Definition of highly resistant gram-negative non-fermenters							
Gram-negative non-fermenters	Ceftazidime	Quinolones	AG	Carbapenems	Piperacillin	Co-trimoxazole	
<i>Acinetobacter</i> spp.	B	B	B	A	N/A	N/A	
<i>Stenotrophomonas maltophilia</i>	N/A	N/A	N/A	N/A	N/A	A	
Other (including <i>Pseudomonas aeruginosa</i> )	C	C	C	C	C	N/A	
Definition of Gram-positive cocci							
Gram-positive cocci	Penicillin					Vancomycin	
<i>Streptococcus pneumoniae</i>	A					A	
<i>Enterococcus faecium</i>	B					B	

AG, aminoglycosides; ESBL, extended-spectrum beta-lactamase; N/A: not applicable. A: resistance against an antibacterial agent from one of the indicated groups of this category is sufficient to define the microorganism as highly resistant. B: resistance against antibacterial agents from at least two of the indicated groups of this category is required to define the microorganism as highly resistant. C: resistance against antibacterial agents from at least three of the indicated groups of this category is required to define the microorganism as highly resistant.

<sup>a</sup> Isolation only indicated for patients in the intensive care unit.



**Figure 1.** Multi-drug resistant organisms (MDRO) alerts. ICU, intensive care unit; MRSA, *meticillin-resistant Staphylococcus aureus*; Q1, questionnaire 1; Q2, questionnaire 2; VZV, varicella zoster virus.

when an MDRO was cultured or when a patient with a previously known MDRO was admitted to hospital. All inpatient adults  $\geq 18$  years of age colonized with an MDRO were eligible for inclusion. Exclusion criteria were: unable to understand or respond in Dutch; terminal illness or otherwise too ill to complete the questionnaire; isolation measures applied for  $<3$  days (shorter periods of isolation were not considered likely to lead to stigmatization); patient required protective or contact isolation for other reasons. The initial goal aim was to recruit 140 participants, with the expectation that approximately 100 would complete the questionnaires [22]. At a standard planned interim analysis after 6 months, the data showed a very low frequency of self-reported stigma, it was considered that further recruitment of patients was highly unlikely to alter the findings and the study was therefore halted after recruiting 41 participants.

### MDRO identification and study definitions

MDROs, as defined by the National coordination of infectious disease control (LCI) [2] (Table 1) were identified, and antibiotic susceptibilities determined, using the VITEK2 system and E-tests where required (BioMerieux, Brussels, Belgium). Minimum inhibitory concentration (MIC) breakpoints for resistance were based on the European Community on Antimicrobial Susceptibility Testing (EUCAST) criteria [23]. Routine MDRO screening was performed only in patients at risk for MDRO colonization, e.g., recent admission to a foreign hospital, or at admission to any intensive care unit, transplantation or haematology ward. Contact duration days were calculated as the time between the start of isolation measures and the day of

discharge or discontinuation of isolation measures because of repeated negative cultures (e.g., loss of colonization).

### Questionnaires

Potential participants were recruited during their hospital stay and informed about the study by a member of the research team. Participants received two questionnaires: a 28-item in-hospital questionnaire that was handed over by a member of the research team after a minimum of three days' isolation, and a 46-item questionnaire sent to the home addresses of the participant two weeks after discharge. Questionnaires were returned in a sealed envelope to a member of the research team, who was not involved in the care of the participants.

The 28-item questionnaire included 14 items relating to patient characteristics, duration of carrier status and experiences with isolation precautions. The remaining 14 items concerned HCW interactions and were derived from the Consumer Quality Index questionnaire (CQI), developed and validated by the Dutch Institute for research in primary care (NIVEL) [24]. The CQI is a 91-item standardized instrument to identify the quality of care from a patient perspective. This instrument is based on the international HCAHPS Survey, a questionnaire frequently used in previous studies to measure the effect of isolation precautions on patient satisfaction [25]. Specific CQI items were selected to focus on patient–provider interaction topics, such as communication and information provision. Most CQI questions were asked using a four-point Likert scale (never, sometimes, mostly and always), and attributed one, two, three and four points with each following answer (reverse scoring in negatively formulated questions).

The remaining questions were assigned points according to the number of possible answers. The higher the overall score, the better the perceived quality of care and interaction between MDRO carrier and HCWs. The CQI items in the context of this study were not selected to assess the effect of isolation on quality of care, but to evaluate whether MDRO-related stigma was confounded by this interaction.

The second questionnaire included questions about stigma and mental health. Stigma was measured using the recently translated and modified 40-item Berger Human Immunodeficiency (HIV) stigma scale (four-point Likert Scale) for MRSA [22,26,27]. Mental Health was measured using the five-item RAND Mental Health Inquiry (six-point scale) [28].

At the end of each questionnaire an open question was added for 'any other comments': this inclusion can increase the quality of obtained data and improve response rates [29]. A systematic content analysis of supplementary comments was

performed by two authors according to the method proposed by O' Cathain et al. [30]. Comments were translated into English by the research team, and clustered according to theme.

### Statistical analysis

Data about sex, age and type of MDRO were collected from the patient electronic medical files. Median CQI, stigma- and RAND score were calculated for each patient characteristic and compared using non-parametric tests (Mann–Whitney *U*-test or

**Table II**  
Consumer Quality Index questionnaire (CQI analysis): median CQI score for each patient characteristic

N = 38	N (%)	Median CQI score	SD
<b>Sex<sup>a</sup></b>			
Male	26 (68.4)	58.5	7.2
Female	12 (31.6)	59.5	5.0
<b>Age (years)<sup>b</sup></b>			
<40	1 (2.6)	62	—
40–60	11 (28.9)	61	4.8
60–80	20 (52.6)	58	7.6
≥80	6 (15.8)	61	4.7
<b>Educational level<sup>b</sup></b>			
Low	7 (18.4)	58	3.7
Middle	13 (34.2)	61	5.6
High	18 (47.4)	57.5	7.7
<b>Household setting<sup>a</sup></b>			
Single person	3 (7.9)	56	6.1
Multiple persons	35 (92.1)	60	6.5
<b>Chronic illness<sup>a</sup></b>			
No	16 (42.1)	60	5.2
Yes	22 (57.9)	58.5	7.4
<b>Type of MDRO<sup>b</sup></b>			
Enterobacterales ESBL+	15 (39.5)	60	5.5
Enterobacterales ESBL-	11 (28.9)	59	9.6
<i>Pseudomonas</i> spp., CPE-	1 (2.6)	58	—
VRE	1 (2.6)	50	—
Polymicrobial	8 (21.1)	58	3.8
Other	2 (5.3)	61	1.4
<b>Previously known or new carrier<sup>b</sup></b>			
Previously known	20 (52.6)	59	7.9
New carrier	16 (42.1)	59	4.9
Previously known but additional MDRO	2 (5.2)	59.5	2.1

CPE, carbapenemase-producing Enterobacterales; ESBL, extended-spectrum beta-lactamase; MDRO, multi-drug resistant organism; SD, standard deviation; VRE, vancomycin-resistant *Enterococcus faecium*. Polymicrobial: colonization with ≥2 MDROs. Chronic illness is defined as an illness for which a hospital is visited at least once per year.

<sup>a</sup> No statistically significant difference observed in medians using the Mann–Whitney *U*-test in case of two groups.

<sup>b</sup> The Kruskal–Wallis test >2 groups.

**Table III**  
Stigma/RAND analysis: median stigma and RAND mental health score for each patient characteristic

N = 31	N (%)	Median stigma score	SD	Median RAND score	SD
<b>Sex<sup>a</sup></b>					
Male	21 (67.7)	64	18.0	84	19.6
Female	10 (32.3)	60.5	20.3	90	25.7
<b>Age (years)<sup>b</sup></b>					
<40	1 (3.2)	82	—	92	—
40–60	10 (32.3)	67	18.8	82	24.6
60–80	15 (48.4)	58	18.7	80	22.0
≥80	5 (16.1)	50	16.3	92	3.6
<b>Educational level<sup>b</sup></b>					
Low	6 (19.4)	61.5	19.0	82	20.2
Middle	13 (41.9)	66	20.8	92	28.3
High	12 (38.7)	55	14.1	86	12.0
<b>Household setting<sup>a</sup></b>					
Single person	2 (7.5)	81.5	23.3	50	42.4
Multiple persons	29 (93.5)	62	18.1	88	18.7
<b>Chronic illness<sup>a</sup></b>					
No	14 (45.2)	56	13.9	86	12.7
Yes	17 (54.8)	68	20.9	88	26.6
<b>Type of MDRO<sup>b</sup></b>					
Enterobacterales ESBL+	13 (41.9)	58	12.1	88	15.1
Enterobacterales ESBL-	8 (25.8)	82	20.6	72	32.3
<i>Pseudomonas</i> spp., CPE-	1 (3.2)	40	-	100	-
VRE	1 (3.2)	49	-	68	-
Polymicrobial*	6 (19.4)	61.5	19.1	88	13.1
Other	2 (6.5)	65.5	23.3	96	5.7
<b>Previously known or new carrier<sup>b</sup></b>					
Previously known	17 (54.8)	66	20.9	88	25.9
New colonization	12 (38.7)	56	14.8	90	15.4
Previously known but additional MDRO	2 (6.5)	73	12.7	82	2.8

CPE, carbapenemase-producing Enterobacterales; ESBL, extended-spectrum beta-lactamase; MDRO, multi-drug resistant organism; SD, standard deviation; VRE, vancomycin-resistant *Enterococcus faecium*. Polymicrobial: colonization with ≥2 MDROs. Chronic illness defined as an illness for which a hospital is visited at least once per year. Clear stigma (110–160), suggestive of stigma (75–109), no stigma (40–74), Poor mental health (≤60), good mental health (>60).

<sup>a</sup> No statistically significant difference observed in medians using the Mann–Whitney *U*-test in the case of two groups. Statistically significant defined as  $P < 0.05$ .

<sup>b</sup> The Kruskal–Wallis test >2 groups.

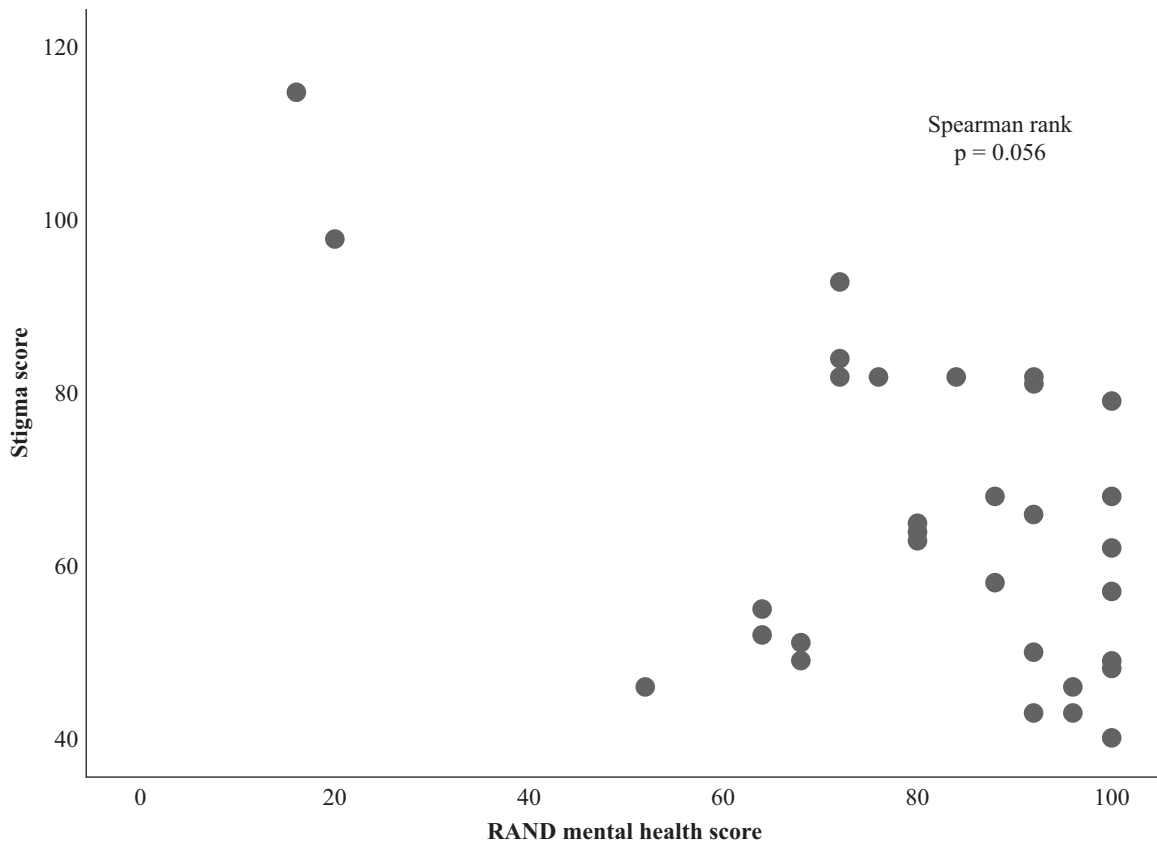


Figure 2. Scatterplot correlation of Stigma Score and RAND Mental Health score.

Kruskall–Wallis test depending on the number of groups). The CQI score was calculated as the sum of the score of each question with a range of 12–67 points. In two of 14 items the participants could rate their HCWs from 0 to 10 points, with 10 points indicating ‘excellent’. Hence the minimum score of 12 points. The translated Berger Stigma Scale for MRSA consists of 40 questions. Stigma scores were calculated as per instruction (range 40–160 points). Stigma scores are categorized into ‘no stigma’ (score 40–74), suggestive for stigma (score 75–109) and clear stigma (110–160). Items that were missing in the questionnaire were replaced with the individual mean by imputing the mean for cluster questions according to Shrive *et al.* [30]. RAND mental health scores were calculated as per instructions as well, based on comparison with the Mental Health Inventory (MHI)-5 scoring system. This scoring system is used to determine whether there is poor mental health based on five questions about feelings of happiness, sadness and fear. The total score was categorized as ‘poor mental health’ (score  $\leq 60$ ) or ‘good mental health’ (score  $> 60$ ). The Spearman rank correlation test was used to assess whether there was a correlation between stigma and CQI scores. This test was also used to calculate the association between stigma and RAND mental health scores. All statistical analyses were performed using SPSS V 23.0. statistical software package.

### Ethical approval

The study was approved by the Leiden University Medical Center (LUMC) institutional ethical review board. Participants were enrolled after informed consent was obtained by the

study coordinator. Patient data were anonymized in the final databases.

## Results

### Population characteristics

A total of 639 alerts for 330 MDRO carriers were sent during the study period from 1<sup>st</sup> September until 28<sup>th</sup> February 2019. Two-hundred and eighteen MDRO carriers were potentially eligible for inclusion. *Escherichia coli* was the most observed MDRO ( $N = 133$ , 61%), followed by *Klebsiella* spp. ( $N = 32$ , 14.7%). Twenty-four (11%) cases were polymicrobial. Extended-spectrum beta-lactamase (ESBL) was found in 65.6% ( $N = 143$ ) MDRO carriers, and there were nine vancomycin-resistant *Enterococcus faecium* (VRE) alerts (4.2%). No carbapenemase-producing Enterobacterales (CPE) were found, but there was one carbapenemase-producing *Pseudomonas aeruginosa*. Ultimately, 60 MDRO carriers met all inclusion criteria, and 41 of these agreed to participate in the study. The most common reason for exclusion was isolation for  $< 3$  days. A total of 50 MDROs were detected amongst the 41 consenting patients (*E. coli* 58%; *K. pneumoniae* in 26%; ESBL 56%; VRE 2%). Ten cases had an active infection with an MDRO; the remaining 31 patients were asymptotically colonized. Median contact duration was 12 days (standard deviation 10.75). The majority (97.6%) of 41 participants were assigned to contact isolation. The remaining participant (2.4%) received care while in contact plus airborne isolation because of colonization with *Acinetobacter* spp. Thirty-eight of 41 initial questionnaires and 31

**Table IV**  
Systematic content analysis of supplementary comments

Issues (N = 38)	N	Illustrative comment	Points of improvement
Organizational barriers	8	"The precautions are trivialized by the personnel"	Education of HCWs
		"...Hand gloves were not always used according to protocol."	Training of HCWs
		"Health personnel do not fully understand how the precautions work in case of a MDRO, there seems to be no clear protocol and I had to say that I have a MDRO repeatedly, which I do not like."	Education and training of HCW and communication
		"I have experienced that different departments address the contact precautions in a different manner."	Training of HCWs
		"The communication between physician and nurses about the implementation of contact precautions should be better."	Communication
Lack of patient centeredness	1	"Little information is given to the patient which gives the impression that it is not taken seriously"	Communication
Blaming of the hospital	1	"At the policlinic I have to tell the physicians myself that I have a MDRO"	Communication/notification
Socio-political context	1	"There should be more publicity about MDROs, so that everyone knows it could happen to them without feeling all the responsibility for it"	Public awareness
Issues already addressed	14	"People avoid me, because they think I am contagious"	Education and training of HCWs and communication
		"Nobody told me about the presence of a MDRO during my hospital stay, therefore I was unaware of the risks."	
		"It never bothered me"	
		"I think it is a private issue, and I don't have to tell others about it"	
Issues not concerning MDRO	13	—	

HCW, healthcare workers; MDRO, multi-drug resistant organism.

second questionnaires were completed (Figure 1). Nine patients did not respond to repeated reminders to complete the questionnaire(s), and one declined to complete the questionnaires because they felt that the CQI questions did not apply to the carrier state.

### Perception of care

Ten carriers (24.4%) indicated that they did not receive sufficient information from HCWs about the specific MDRO colonization. Thirteen carriers (31.7%) reported they did not receive sufficient information about the contact precautions. The CQI analysis was performed in 38 participants. The median CQI score was 59 (interquartile range 6), indicating good quality of care (Table II).

### Reported stigma and RAND mental health

Stigma and RAND mental health analysis were performed in 31 MDRO carriers. Most participants (67.7%) did not experience

stigma (score <75). Nine carriers (29%) had an adjusted Berger score of 75–109 suggesting stigma and one MDRO carrier scored 115 points indicating clear stigma. When observing the total RAND mental health score, 28 persons (90.3%) were considered to have 'good mental health' and three persons (9.7%) had a score  $\leq 60$  indicating 'poor mental health' (Table III).

### Stigma: association with mental health and perception of care

There was no correlation between stigma score and RAND mental health score (Spearman correlation coefficient -0.347 ( $P=0.056$ )) and stigma score and perception of care (Spearman correlation coefficient -0.201 ( $P=0.28$ )) (Figure 2).

### Analyses of supplementary comments

The 'any other comments' section of both questionnaires resulted in 33 comments. Thirteen comments did not concern MDRO or the isolation measures and were therefore excluded.

Most new issues concerned organizational barriers (Table IV). In eight comments, participants stated that it appeared that HCWs lacked knowledge about contact precautions.

## Discussion

In this quantitative questionnaire study, MDRO colonization was not clearly associated with stigma, in contrast to general experience with MRSA [13,16,17,19,22,31–33]. Actions to prevent transmission of MRSA, such as isolation and intensive MRSA eradication therapy, seem to result in higher stigma scores, which in turn are associated with poor mental health. In a recent literature review by Rump *et al.*, carriage and rate control measures were found to interfere with quality of care and cause stigmatization; 21 of the 27 studies in this systematic review related to MRSA carriers [14].

How can the difference in the results observed in this study compared with the results in previous MRSA studies be explained? One reason could be that MRSA is associated with more extended isolation precautions and more intensive eradication therapy, whereas other MDROs require only contact precautions that are not as visible to the patient. Isolation precautions for MRSA have been used for a longer period of time, meaning that people have more (negative) knowledge about it. In the Netherlands, contact plus airborne isolation precautions are required for MRSA, which includes mask wearing and door closure, whereas for most other MDROs HCWs do not wear masks and doors can remain open. A recent review of the impact of MDROs showed that the negative impact of MRSA goes beyond the healthcare setting, and touches upon many aspects of human life. Other MDROs are relatively new and less well-known to the public and may therefore (so far at least) impact less outside hospital settings [34].

Isolation precautions can result in less direct patient contact, because each contact is more time consuming. Previous studies have shown that HCWs may want to avoid confronting the impact of psychological effects of isolation [13,14,17,22]. This study shows the interaction with HCWs was overall interpreted as 'good', with a median CQI score of 59. This overall good perception of healthcare is in contrast with most studies on MDRO experiences and may have led to less stigma. A concerning finding in this context is that participants often described that the HCWs failed to provide them with enough information about their MDRO carrier status. Also, they observed a lack of compliance by HCWs with contact precautions; indeed, some carriers reported being sometimes better informed about their carrier status, and to take it more seriously, than HCWs caring for them. This is problematic for two reasons. First, because having unanswered thoughts and questions negatively impacts on wellbeing; indeed, other studies have shown that MDRO carriers struggle with comprehending their situation [14]. Second, lack of compliance by HCWs negatively impacts the effectiveness of MDRO control measures, which is a highly unwanted situation [13,32]. Therefore, adequate training of HCWs is warranted, including better provision of information towards patients [35].

Contact precautions have been associated with negative results on the emotions of the carrier. They may feel more depressed, resulting in stress or isolation [4–14]. In this study there was no correlation of stigma score with RAND mental health score of the carriers. This may be the consequence of

the small sample size and the low prevalence of stigma. Some cases, however, added a comment that showed that they felt some kind of isolation or experienced lack of patient centeredness during hospitalization.

An important strength of this study is its quantitative design compared with the previous studies that are primarily based on qualitative designs [13,14,36]. A limitation is the sample size of the study. The early halt was however instigated by interim analysis of the data. To detect causality between RAND mental health scores or experienced quality of care with reported stigma remains difficult. Patients with MDROs frequently are hospitalized patients with a chronic disease. The chronic disease may influence their experiences of stigma or their mental health. A standardized stigma scale was used instead of developing a new one because this has important methodological advances. One could argue that MRSA as an outpatient potentially has more relevance to the used HIV stigma scale than for other MDROs.

In contrast to previous studies mainly concerning MRSA, MDRO-related stigma was limited in this quantitative study. Colonization with an MDRO, and the required isolation precautions, did not result in clear stigma. When subjecting people to infection control measures, potential negative impact on their wellbeing remains a major issue of concern. The results of this study, however, suggest that currently in the case of MDRO control measures, prevention of stigma does not need to be our primary focus. This is an important result the view of the increasing number of MDRO carriers and (consequently) the importance of isolation measures.

The following conclusions can be drawn from this study: contact precautions for MDRO were not clearly associated with stigma; carriers should receive appropriate information about the MDRO from their HCWs; the findings support the importance of consequent adherence to contact precautions. More research is needed to investigate the association between stigma and MDRO colonization or infection in other settings, geographical areas, as well as its development of stigma over time.

## Acknowledgements

The authors thank all respondents for participation in this study and M. L. Bruijning (MSc, Department of Infection Prevention), for help in identifying potential participants for this study.

### Conflict of interest statement

None declared.

### Funding sources

Funding was provided by the Ministry of Health, Welfare and Sport.

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