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ORIGINAL ARTICLE

Carbapenem-Resistant *Klebsiella pneumoniae* in Post-Acute-Care Facilities in Israel

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OBJECTIVE. To assess the prevalence of and risk factors for carbapenem-resistant *Klebsiella pneumoniae* (CRKP) carriage among patients in post-acute-care facilities (PACFs) in Israel.

DESIGN, SETTING, AND PATIENTS. A cross-sectional prevalence survey was conducted in 12 PACFs. Rectal swab samples were obtained from 1,144 patients in 33 wards. Risk factors for CRKP carriage were assessed among the cohort. Next, a nested, matched case-control study was conducted to define individual risk factors for colonization. Finally, the cohort of patients with a history of CRKP carriage was characterized to determine risk factors for continuous carriage.

RESULTS. The prevalence of rectal carriage of CRKP among 1,004 patients without a history of CRKP carriage was 12.0%. Independent risk factors for CRKP carriage were prolonged length of stay (odds ratio [OR], 1.001; $P < .001$), sharing a room with a known carrier (OR, 3.09; $P = .02$), and increased prevalence of known carriers on the ward (OR, 1.02; $P = .013$). A policy of screening for carriage on admission was protective (OR, 0.41; $P = .03$). Risk factors identified in the nested case-control study were antibiotic exposure during the prior 3 months (OR, 1.66; $P = .03$) and colonization with other resistant pathogens (OR, 1.64; $P = .03$). Among 140 patients with a history of CRKP carriage, 47% were colonized. Independent risk factors for continued CRKP carriage were antibiotic exposure during the prior 3 months (OR, 3.05; $P = .04$), receipt of amoxicillin-clavulanate (OR, 4.18; $P = .007$), and screening within 90 days of the first culture growing CRKP (OR, 2.9; $P = .012$).

CONCLUSIONS. We found a large reservoir of CRKP in PACFs. Infection-control policies and antibiotic exposure were associated with patient colonization.

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The spread of multidrug-resistant microorganisms in health care facilities has resulted in increasing morbidity, mortality, and cost of care.¹ Prevention of the emergence of resistance and the dissemination of resistant microorganisms has become a major public health priority. Numerous reports have indicated that antimicrobial resistance is commonly encountered in long-term-care facilities (LTCFs), which may act as reservoirs and amplifiers of resistant organisms.²⁻⁵ Most isolation guidelines have targeted acute-care settings^{6,7} and may not be suitable or effective in LTCFs. LTCF residents remain in the facility for prolonged periods of time, share common eating and rehabilitation areas, and participate in common activities. Implementing infection-control measures that are identical to those in an acute-care setting may result in less effective rehabilitation as well as undesirable psychological and social consequences. Furthermore, data on the effectiveness of infection-control measures in LTCFs are limited.⁸

In recent years, carbapenem-resistant *Klebsiella pneumoniae* (CRKP) have spread, achieving high rates of prevalence

in health care facilities in various geographical areas.⁹⁻¹² CRKP account for approximately 10% of all *K. pneumoniae* infections reported from across the United States to the National Healthcare Safety Network¹³ and one-quarter of all invasive *Klebsiella pneumoniae* infections reported from New York.¹⁴ Infections with CRKP are associated with increased morbidity and mortality; indeed, patients with CRKP infection are approximately 3 times more likely to die during their hospital stay than patients with susceptible strains.¹⁴⁻¹⁶ The spread of these resistant organisms has been recognized as a major threat to the public health.^{7,17,18}

Since 2006, an epidemic clone of *K. pneumoniae* carbapenemase (KPC)-producing CRKP has been spreading in acute-care hospitals in Israel, infecting 185 new patients per month at the peak of the outbreak, in March 2007.¹⁹⁻²² In response, a nationally directed infection-control program was implemented in all acute-care facilities in the country, leading to a dramatic decrease in the incidence of new cases of nosocomial CRKP in acute-care facilities.²² During 2008, ap-

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TABLE 1. Descriptive Characteristics of the 1,144 Patients Screened for Carriage of Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP)

Characteristic	Value
Male sex	517 (45.6)
Mean $\pm$ SD (range) age, years	72.9 $\pm$ 15.9 (7–101)
Ward type	
Skilled nursing care	357 (31.8)
Chronic mechanical ventilation	162 (14.2)
Rehabilitation	375 (32.8)
Subacute	250 (21.9)
Median (IQR, range) days before screening	44 (165, 0–4,514)
Prior history of colonization with CRKP	140 (12.2)
Infection-control policies	
CRKP screening on admission	129 (11.3)
Cohorting of colonized patients	188 (16.4)

NOTE. Data are no. (%) of patients, unless otherwise indicated. IQR, interquartile range; SD, standard deviation.

proximately 30% of patients infected or colonized with CRKP were discharged from acute-care facilities to LTCFs, resulting in a substantial potential carrier reservoir in these facilities. Moreover, patients admitted to acute-care hospitals from LTCFs were frequently found to be carriers of CRKP on admission surveillance.

The Israel National Center for Infection Control performed this survey in order to determine a policy for the containment of CRKP in LTCFs. Here we aimed to assess the prevalence of CRKP carriage among residents of post-acute-care facilities (PACFs) in Israel and to characterize institutional as well as individual patient risk factors for CRKP infection. We also assessed risk factors for continued CRKP colonization among patients with a history of carriage.

METHODS

Study Size, Subjects, and Design

A cross-sectional prevalence survey was conducted from November 2008 to January 2009 in 12 of the 13 PACFs in Israel. These facilities provide continued intensive treatment after hospital discharge to patients with conditions that result in reduced ability to perform activities of daily living. Wards are classified as skilled nursing care, chronic mechanical ventilation, sub-acute, and rehabilitation. A 1-day point-prevalence study was performed in a representative sample of wards, determined by the random selection of 1 of each type of ward existing in each facility. In each ward studied, all patients were included.

We performed 2 analyses directed at new detection of CRKP carriage. The first analysis aimed to define institutional, ward, and patient characteristics associated with increased risk of CRKP carriage among the entire cohort of patients without a history of CRKP carriage. In the second analysis, we conducted a nested case-control study to further define individual risk factors for CRKP carriage. Case patients were defined as those with no history of CRKP carriage and with a positive

screening culture result. Control patients were those with negative screening culture results. Case patients were matched to control patients by ward (group-level matching). In addition, a third analysis was conducted that was directed at all patients with a history of CRKP carriage. In this analysis, we assessed risk factors for continued colonization.

Data Collection

The characteristics of the LTCFs and the demographic data of their patients were collected, using structured questionnaires. The following data were collected for all patients: age, sex, date of admission to the facility, type of ward, known previous CRKP colonization, and sharing a room with a known carrier. The following characteristics were collected for the facilities: prevalence of CRKP carriers in each ward and infection-control policies (active surveillance for carbapenem-resistant *Enterobacteriaceae* carriage on admission, isolation policy for carriers, dedicated nursing staff for CRKP carriers).

For patients included in the nested case-control study and for patients with a past history of CRKP carriage, additional data were collected from medical records, including underlying diseases, Charlson comorbidity index score,²³ Norton score (a scale for assessing the risk of developing decubitus ulcers),²⁴ presence of decubitus ulcers, invasive devices, colonization with other multidrug-resistant organisms, antibiotic use within the past 3 months, and hospital stay during the past 6 months.

Microbiologic and Molecular Methods

Rectal swab samples were collected and plated directly by rolling the swab several times onto CHROMagar KPC plates (HyLabs) and then inoculating the sample into 5 mL of brain-heart infusion enrichment broth (HyLabs). We chose CHROMagar KPC plates as a screening medium because of the high sensitivity and specificity of this medium and its

TABLE 2. Risk Factors for Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP) Carriage among the Cohort of 1,004 Patients with No Prior History of Colonization

Characteristic	CRKP-noncolonized patients (<i>n</i> = 883)		CRKP-colonized patients (<i>n</i> = 121)		Univariate analysis		Multivariable analysis	
					OR (95% CI)	<i>P</i>	Adjusted OR (95% CI)	<i>P</i>
Mean (SD) age, years	73.0 (15.5)		72.8 (17.6)		1 (0.99–1.01)	.94		
Male sex	401 (45.8)		51 (42.1)		1.16 (0.79–1.71)	.44		
Median (IQR) days before screening	33 (119)		138 (549)		1.001 (1.001–1.001)	<.001	1.001 (1.001–1.001)	<.001
Sharing a room with a known CRKP carrier	28 (3.2)		14 (11.6)		3.98 (2.04–7.80)	<.001	3.09 (1.52–6.23)	<.001
Average prevalence of known CRKP carriers in ward (SD)	8.72 (12.7)		13.3 (15.5)		1.02 (1.01–1.04)	.08	1.02 (1.004–1.033)	.013
Type of ward								
Chronic mechanical ventilation	111 (12.6)		15 (12.4)		1	<.001		
Skilled nursing care	215 (24.3)		75 (62)		2.58 (1.42–4.7)			
Rehabilitation	350 (39.6)		9 (7.4)		0.19 (0.08–0.45)			
Subacute	207 (23.4)		22 (18.2)		0.79 (0.39–1.58)			
Cohort policy	139 (15.7)		22 (18.2)		1.19 (0.72–1.95)	.5		
Screening policy	95 (10.8)		7 (5.8)		0.51 (0.23–1.16)	.08	0.41 (0.18–0.93)	.03

NOTE. Data are no. (%) of patients, unless otherwise indicated. CI, confidence interval; IQR, interquartile range; OR, odds ratio; SD, standard deviation.

TABLE 3. Individual Risk Factors for Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP) Carriage among the Nested Case-Control Study Patients with No Prior History of Colonization

Characteristic	CRKP-noncolonized patients (n = 149)		CRKP-colonized patients (n = 118)		Univariate analysis		Multivariable analysis	
					OR (95% CI)	P	Adjusted OR (95% CI)	P
Mean (SD) age, years	74.4 (15.9)		72.6 (18.3)		0.99 (0.99–1.007)	.41		
Male sex	70 (47.0)		47 (39.8)		1.15 (0.77–1.71)	.50		
Bedridden	89 (59.7)		86 (76.7)		0.65 (0.38–1.16)	.12		
Charlson comorbidity index score (SD)	3.89 (2.4)		3.79 (2.4)		1 (0.92–1.09)	.99		
Norton score (SD)	11.28 (3.4)		9.8 (2.9)		0.931 (0.86–1.09)	.08		
Decubitus ulcer	49 (34.0)		60 (51.3)		1.342 (0.9–2.001)	.15		
Nasogastric tube	48 (32.2)		62 (52.5)		1.42 (0.93–2.16)	.10		
Urinary catheter	69 (46.3)		73 (61.9)		1.34 (0.89–2.01)	.15		
Tracheostomy	34 (22.8)		39 (33.1)		1.53 (0.88–2.64)	.13		
Colonized with other MDRO	25 (16.8)		40 (33.9)		1.79 (1.16–2.76)	.008	1.64 (1.06–2.55)	.03
Antibiotic exposure during prior 3 months	87 (58.4)		94 (79.7)		1.8 (1.13–2.86)	.01	1.66 (1.04–2.66)	.03
Receipt of amoxicillin-clavulanate during prior 3 months	24 (16.1)		35 (29.7)		1.5 (0.95–2.37)	.08		
Receipt of fluoroquinolone during prior 3 months	31 (20.8)		35 (29.7)		1.4 (0.92–2.14)	.12		
Receipt of cephalosporin during prior 3 months	55 (36.9)		54 (45.8)		1.31 (0.87–1.96)	.20		
Receipt of piperacillin-tazobactam during prior 3 months	0 (0)		2 (1.7)		2.49 (0.54–11.60)	.11		

NOTE. Data are no. (%) of patients, unless otherwise indicated. The following covariates were also assessed, with no significant statistical differences found between the groups: congestive heart failure, dementia, chronic renal failure, diabetes mellitus, malignancy, peripheral vascular disease, stroke, status following multiple traumas, length of stay before screening, intravascular catheter, hospitalization in an acute-care facility during the prior 6 months. CI, confidence interval; IQR, interquartile range; OR, odds ratio; MDRO, multidrug-resistant organism; SD, standard deviation.

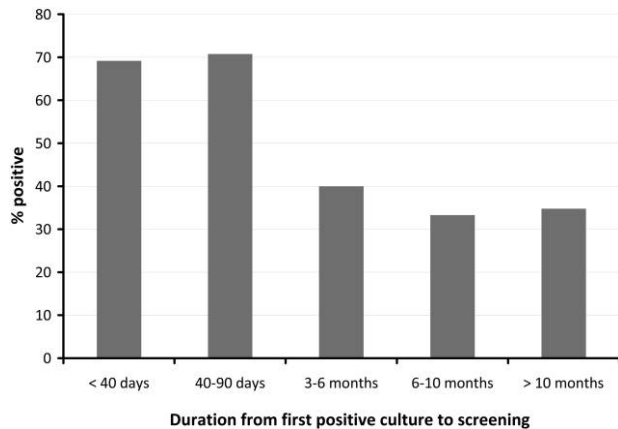


FIGURE 1. Relationship between the timing of screening relative to the first positive carbapenem-resistant *Klebsiella pneumoniae* culture result and continued colonization.

ease of use in CRKP detection.²⁵ Metallic-blue CRKP colonies that were visualized after 24 hours of incubation at 37°C were subcultured onto MacConkey agar plates (PD-032, HyLabs) and introduced into the Vitek-2 automated system (bioMérieux), using the AST-GN09 card for identification and susceptibility testing. After primary analysis, all bacteria identified as CRKP by Vitek-2 were stored at –80°C for further analysis if necessary. Samples that resulted in the growth of CRKP that possessed a typical antimicrobial resistance pattern (resistance to all antibiotics except for an aminoglycoside and colistin) were considered to have positive results. Isolates of *Klebsiella pneumoniae* exhibiting carbapenem resistance but with an atypical susceptibility profile as detected by Vitek-2 (eg, discrepant carbapenem susceptibilities, susceptibility to additional antimicrobial classes) were subjected to *bla*_{KPC} polymerase chain reaction (PCR) testing, using the primers and conditions described previously.²⁶ PCR was also performed when a discrepancy was found between CHROMagar and Vitek, that is, growth of colonies on CHROMagar but the CRKP not identified by Vitek. In addition, enrichment broths from known CRKP carriers that yielded no growth on CHROMagar were subjected to PCR testing. Isolates or broths yielding a positive PCR result were considered to be CRKP positive, whereas those yielding a negative result were considered to be CRKP negative.

Statistical Methods

The data were analyzed with SPSS, version 17.0. Normally distributed continuous variables were compared with the Student *t* test, and nonnormally distributed continuous variables were compared with the Wilcoxon rank sum test. The χ^2 or the Fisher exact test was used to compare categorical variables. The impact of ward type on the risk of CRKP colonization was assessed by comparing risk in skilled nursing, rehabilitation, and subacute wards with that in the chronic mechan-

ical ventilation wards, which was used as a reference. Multivariable regression models were constructed, using a stepwise approach. For model building, parameters with a *P* value of at most .1 between groups in the univariate analysis were entered into the model. In the multivariable analysis, variables with a *P* value of at most .05 were considered to be significant. All *P* values in this study were 2-tailed.

For the matched case-control study, each variable was tested in the case and control groups by use of bivariate conditional logistic regression to look for an association with CRKP acquisition. Variables in this analysis that were associated with CRKP acquisition and that had *P* values of at most .10 were entered into a multivariable conditional logistic regression model. Approval for the study was obtained from the Research Ethics Committee of the Tel Aviv Sourasky Medical Center, the jurisdictional ethical review board.

RESULTS

Characteristics of the Facilities and Patients

Of the 13 PACFs in Israel, 12 were included in the study, for a total of 2,451 beds (median, 209; range, 104–320). Isolation practices varied. Eleven PACFs indicated that they isolated or cohorted patients who were carriers of CRKP. In 1 facility, colonized patients shared rooms with noncolonized patients. Two facilities cohorted all colonized patients in dedicated wards that had dedicated nursing staffs (ie, nurses caring for carriers would not be assigned to noncarriers on the same shift), and this required that patients be isolated in their rooms at all times. The other 10 PACFs implemented modified contact precautions and permitted colonized patients to perform individual or group activities in common areas. Two facilities screened newly admitted patients for carriage of CRKP, placing those found to be carriers under modified contact precautions.

We conducted the point-prevalence survey in 33 wards. A total of 1,144 residents, 46.7% of the total number of PACF patients, were screened. Table 1 describes the characteristics of the study population. The mean ($\pm$ standard deviation [SD]) age of the study population was 72.9 ($\pm$ 15.9) years. The median length of stay in the PACFs was 44 days (interquartile range [IQR], 165 days; range, 0–4,514 days). One hundred and forty patients (12.2%) had a prior history of CRKP colonization. Among all patients screened, CRKP carriage was detected in 16.3% (187 of 1,144).

Risk Factors for Rectal Carriage among Patients without History of CRKP Carriage

The prevalence of rectal carriage among patients without a history of CRKP carriage was 12.0% (121 of 1,004), and it varied among the institutions, ranging from 2.1% to 28.6%. Prevalence differed between ward types: it was 25.9% (75 of 290 patients; range, 0%–66%) in the skilled nursing care ward, 11.9% (15 of 126 patients; range, 0%–25%) in the

TABLE 4. Risk Factors for Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP) Carriage among 128 Patients with a Prior History of Colonization

Characteristic	CRKP-noncolonized patients (n = 63)		CRKP-colonized patients (n = 65)		Univariate analysis		Multivariable analysis	
					OR (95% CI)	P	Adjusted OR (95% CI)	P
Mean (SD) age, years	72.7 (16.0)		73.5 (15.7)		0.77 (0.98–1.03)	.77		
Male sex	26 (41.3)		29 (44.6)		0.87 (0.43–1.76)	.70		
Median (IQR) days before screening	201 (336)		128 (218.5)		0.99 (0.99–1)	.095		
Median (IQR) days from first positive culture	189 (196)		76.5 (164.8)		0.99 (0.99–0.99)	.001		
Screening within 90 days of first positive culture result	15 (23.8)		33 (53.2)		3.64 (1.69–7.82)	.001	2.86 (1.25–6.52)	.012
Bedridden	45 (73.8)		50 (82.0)		0.62 (0.26–1.43)	.28		
Norton score (SD)	9.95 (2.8)		9.72 (2.7)		0.97 (0.85–1.11)	.64		
Charlson comorbidity index score (SD)	3.35 (2.23)		3.66 (2.62)		1.06 (0.91–1.22)	.47		
Intravascular catheter	23 (36.5)		39 (60.0)		2.61 (1.28–5.33)	.008		
Tracheostomy	33 (52.4)		21 (32.3)		0.43 (0.21–0.89)	.02		
Urinary tract catheter	40 (63.5)		41 (63.1)		0.98 (0.48–2.02)	.96		
Decubitus ulcer	34 (54.0)		37 (56.9)		1.18 (0.56–2.26)	.737		
Hospitalization in acute care facility during prior 6 months	26 (41.3)		41 (63.1)		2.43 (1.19–4.90)	.014		
Antibiotic exposure during prior 3 months	40 (63.5)		59 (90.8)		5.65 (2.11–15.13)	<.001	3.05 (1.08–8.70)	.04
Receipt of amoxicillin-clavulanate during prior 3 months	6 (9.5)		26 (40.)		6.33 (2.38–16.82)	<.001	4.19 (4.48–11.84)	.07
Receipt of a cephalosporin during prior 3 months	21 (33.3)		36 (55.4)		2.48 (1.21–5.08)	.012		
Type of ward								
Skilled nursing care	24 (38.1)		39 (60.0)		2.44 (0.198–4.96)	.013		
Chronic mechanical ventilation	18 (28.6)		11 (16.9)		0.51 (0.22–1.19)	.116		
Rehabilitation	9 (14.3)		7 (10.8)		0.724 (0.252–2.08)	.548		
Subacute	12 (19.0)		8 (12.3)		0.596 (0.226–1.58)	.294		
Cohort policy	10 (15.9)		24 (36.9)		0.32 (0.14–0.75)	.007		

NOTE. Data are no. (%) of patients, unless otherwise indicated. The following covariates were also assessed, with no significant statistical differences between the groups: congestive heart failure, dementia, chronic renal failure, diabetes mellitus, malignancy, peripheral vascular disease, stroke, status following multiple traumas, length of stay before screening, nasogastric tube. CI, confidence interval; IQR, interquartile range; OR, odds ratio; SD, standard deviation.

chronic mechanical ventilation ward, 9.6% (22 of 229 patients; range 3%–26%) in the subacute ward, and 2.5% (9 of 359 patients; range, 0%–13%) in the rehabilitation ward.

Table 2 summarizes the characteristics of 121 colonized patients versus those of 883 noncolonized patients. Colonized patients were more likely to be in a skilled nursing ward, have a greater length of stay before screening, share a room with a patient with a history of CRKP colonization, and be located in a ward with a higher prevalence of patients known to be colonized. Patients hospitalized in rehabilitation wards or in a facility with a ward-based policy of screening on admission were less likely to be colonized. In multivariable analysis, independent risk factors for CRKP carriage were greater length of stay (OR, 1.001; $P < .001$), sharing a room with a patient with a prior history of CRKP carriage (OR, 3.09; $P = .02$), and a higher average prevalence of known carriers on the ward (OR, 1.02; $P = .013$). Hospitalization in a facility with a policy of screening on admission was protective against CRKP colonization (OR, 0.41; $P = .03$).

Nested Case-Control Study

Of the 121 patients who had CRKP colonization, medical records were available for 118. These patients were included as case patients. A total of 149 ward-matched controls were randomly selected from the 833 patients who had negative screening culture results. Characteristics of patients included in the nested case-control study are shown in Table 3. Characteristics associated with CRKP in univariate analysis were Norton score, skin lesions, antibiotic exposure during the past 3 months, receipt of amoxicillin-clavulanate during the past month, and colonization with other resistant pathogens. Multivariable analysis identified antibiotic exposure during the past 3 months (OR, 1.66; $P = .03$) and colonization with other multidrug-resistant organisms (OR, 1.64; $P = .03$) as independent risk factors for CRKP colonization.

Risk Factors for Continued Colonization among Past CRKP Carriers

Of the 140 prior CRKP carriers, colonization was detected in 66 (47%). Medical records were available for 128 patients. Among 50 patients screened within 3 months of the first positive culture result, 35 (70%) were CRKP-positive, versus 27 of 75 patients (36%) who were screened after 3 months ($P = .001$). Figure 1 demonstrates the association between timing of screening relative to the first positive CRKP culture and continued colonization. Factors associated with CRKP carriage in univariate analysis were residence in a skilled nursing-care ward, being cohorted with other CRKP carriers, hospitalization in an acute-care facility during the prior 6 months, antibiotic exposure during the prior 3 months, presence of an invasive device, and less time elapsed since the first culture of CRKP (Table 4). In multivariable analysis, the independent risk factors for continued CRKP carriage were antibiotic exposure during the prior 3 months, (OR, 3.05;

$P = .04$), amoxicillin-clavulanate exposure during the prior 3 months (OR, 4.18; $P = .007$), and screening within 90 days of the first positive CRKP culture result (OR, 2.9; $P = .012$).

DISCUSSION

In this multicenter, national survey, we detected a large, mostly unrecognized reservoir of CRKP carriers among hospitalized patients in PACFs. In total, 16.3% of screened PACF patients were carriers of CRKP. About two-thirds of these were previously unknown to be carriers. A wide variation in the prevalence of CRKP colonization was found between institutions and ward types. Rehabilitation wards had the lowest prevalence (3%), while skilled nursing wards were most heavily affected, with a carrier prevalence of 25%.

Local infection-control policies had an impact on the risk of CRKP colonization. Sharing a room with a CRKP carrier was identified as an independent risk factor for CRKP colonization. By contrast, hospitalization on a ward with a policy of screening for CRKP carriage on admission was protective against colonization. These two factors are important, as they are modifiable. Moreover, it is likely that they act in concert; that is, screening on admission allows classification of patients as carriers or noncarriers, and it allows placement of noncarriers in rooms with other noncarriers only.

Several reports have suggested that active surveillance in combination with the use of contact precautions for colonized patients have resulted in a sustainable reduction in the incidence of infections with methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci.^{27,28} By contrast, the role of active surveillance in the control of multidrug-resistant gram-negative bacteria is not well established. Moreover, little has been reported about the impact of active surveillance in LTCFs, and existing data have been generated largely in the setting of local outbreaks.²⁹ Our results suggest that admission screening may have a role in preventing the spread of resistant enteric gram-negative organisms in LTCFs in the context of a widespread and prolonged outbreak.

The nested, matched case-control study that was conducted to recognize within-ward individual risk factors for CRKP carriage identified recent antibiotic exposure as an independent predictor of carriage. The impact of antibiotic exposure on both the risk of multidrug-resistant microorganism acquisition and prolonged duration of colonization is well known. We found that more than 60% of our study population had recently been exposed to antimicrobial therapy. Likewise, a recent study reported a high rate of antimicrobial therapy utilization among residents in PACFs.³⁰ Of note, we found low rates of use of extended-spectrum antibiotics (eg, piperacillin-tazobactam, carbapenems). Nevertheless, we found that the use of standard antimicrobial therapy had a significant impact on the risk of CRKP colonization. We did not assess the appropriateness of antimicrobial therapy in the case-control study. Yet, a number of studies have reported that 25%–75% of antimicrobial therapy in LTCFs is inap-

appropriate.^{30,31} These findings, along with our results, emphasize the importance of antibiotic control programs that are directed at reducing total antibiotic use in LTCFs rather than restricting broad-spectrum antibiotics only.³²

Few studies have assessed the duration of carriage of multidrug-resistant organisms. Another study undertaken among LTCF residents suggested that clearance occurred significantly more often with resistant gram-negative bacilli colonization than with colonization with vancomycin-resistant enterococci or methicillin-resistant *S. aureus*.³³ In this study, among prior CRKP carriers, more than one-half cleared colonization over time. Risk factors for continued colonization were a positive CRKP culture result within the past 3 months and recent antibiotic exposure. After 3 months, the risk of colonization decreased by 50%. There was a likelihood of 0.004 per day that an individual would lose CRKP colonization during the first 10 months. After 10 months, only 30% of patients remained CRKP positive on screening; this proportion seems to persist over time. The above results should be interpreted with caution, as it is difficult to conclude from our study whether a negative screen test implies clearance of carriage or merely a reduction in the number of organisms carried, to below the threshold detection level of the test. In either case, we believe that a negative test result does imply a lower risk of transmission than a positive result.

The pivotal role of LTCFs in the epidemiology of multidrug-resistant organisms has been recognized.³⁴ Colonized patients are frequently transferred between hospitals and LTCFs; thus, LTCFs can act as reservoirs and amplifiers of resistance. The importance of regional, collaborative efforts between acute-care facilities and LTCFs has been demonstrated in a regional infection-control intervention that succeeded in containing the spread of vancomycin-resistant enterococci over a wide area.³⁵

Our study has several potential limitations. As with any surveillance screening test, sensitivity of the test may be limited. In this study, we used both direct plating and broth-enriched culturing to reduce this possible classification bias. Moreover, the screening method we chose has demonstrated very high sensitivity.²⁶ Similarly, cultures were performed only once for patients with a known history of CRKP carriage, and thus we may have missed cases of intermittent carriage. However, among known carriers, the risk of receiving a positive culture result after negative PCR results has been shown to be very low (approximately 5%; Y. Carmeli, unpublished data). We did not measure compliance with hand-hygiene or contact precautions, which may be important, unmeasured confounders. Finally, we could not ascertain whether CRKP acquisition occurred in the PACF or during prior hospitalization in an acute-care facility. In order to determine both the prevalence of imported CRKP and the risk of acquisition in the facility, longitudinal studies are required.

In conclusion, our study detected a large reservoir of CRKP in PACFs in Israel. Admission surveillance cultures for early detection of carriers and implementation of barrier precau-

tions should be part of an infection-control program and must be coordinated between facilities. Antibiotic pressure serves as an important factor in the epidemiology of CRKP in PACFs. Patients transferred from LTCFs to hospitals in regions of high CRKP prevalence should be considered as being at high risk for colonization and should be screened for carriage upon admission. Additional studies to better understand the dynamics of the CRKP reservoir in LTCFs and the direction of the flux of colonized patients between acute-care and chronic-care facilities should be conducted to guide effective infection-control strategies.

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Potential conflicts of interest. The authors report no conflicts of interest relevant to this article.

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