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LESS IS MORE IN INTENSIVE CARE

Less contact isolation is more in the ICU: pro

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Additional contact precautions (ACP) have been endorsed by International Recommendations in patients with colonisation or infection by multidrug-resistant organisms (MDRO) [1, 2]. Contact isolation (CI), considered initially as the holy grail of the interruption of transmission of MDROs, currently remains debated [3, 4]. Suboptimal contact of healthcare personnel with the patients has been associated with service care errors including falls, pressure ulcers, fluid/electrolyte disorders and suboptimal documentation of vital signs or physician notes. Patients' dissatisfaction and stress as well as increased healthcare costs are the major downsides of CI [3]. In view of the divergent opinions in the literature, infection control practices in ICU vary considerably. In this narrative review, we will focus on the most relevant studies, with messages in line with the principle "less is more" (Table 1). In the present manuscript, we considered "less CI" as surrogate to "not universal" or "targeted" CI (and evidently not "no CI"). However, we also discuss studies in which CI seems less important or less effective compared to other pivotal infection control measures, therefore, less desirable. Search methods are shown in Supplement Table.

The efficacy of CI over properly enforced standard precautions with particular focus on adherence to hand hygiene has been questioned. Huskins et al. performed universal screening of patients and then pre-emptive isolation followed by barrier precautions for identified carriers; no significant change in acquisition of MRSA or VRE was demonstrated [4]. Also, Cepeda et al. showed that transfer of MRSA-colonised patients into single rooms or cohorting did not confer to reduced cross-infection [5]

As far as MDR Gram-negative bacteria (MDR-GNB) are concerned, despite international recommendations, no single infection control approach (and particularly not CI) alone was associated with positive outcomes, especially in endemic settings. A recent systematic review and network meta-analysis evaluating (1) standard care (including contact precautions), (2) antimicrobial stewardship, (3) environmental cleaning, (4) source control or (5) decolonization methods for the prevention of multidrug-resistant Gram-negative bacteria (MDR-GNB) in adult Intensive Care Units (ICUs) showed that only four-component strategies adopting components (1)–(5) were effective to prevent MDR-GNB acquisition [6]. Environmental cleaning seems important component for *Acinetobacter baumannii*, whereas decolonization strategy was pivotal in *K. pneumoniae* albeit data derived from low endemicity settings [6]. Sypsa et al. using a Ross-Macdonald model, showed that screening, contact precautions and particularly hand hygiene among a multifaceted infection control bundle (including CI), were the major contributors in the containment of Carbapenemase-producing *Klebsiella pneumonia* in an endemic surgical setting [7]. In this study, cohorting was more common than strict isolation due to intrinsic institutional barriers. Nevertheless, less strict isolation may still prove to be highly effective, provided that contact precautions remain fully functional.

In a prospective multicenter ICU trial by Derde and colleagues, in the context of a rigorous compliance with hand hygiene and universal chlorhexidine body washing, screening and CI of carriers do not reduce acquisition rates of MDRO, irrespective of rapid or conventional screening. However, a reduction in MRSA acquisition was noted [8]. Data from the previous and other studies argue for targeted and non-universal screening and CI measures in endemic environments or outbreaks by ESBL-producing non-*Escherichia coli* Enterobacterales, whereas ESBL-*E. coli* seems to be associated with less CI

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Table 1 Contemporary studies delivering the message "less contact isolation in the ICU is more"

Author, Year	Setting design	Study Size	Target organisms	Intervention	Main outcomes
Studies accessing efficacy of IC measures in MDRO colonization/infection					
Huskins WC et al., 2011 [4]	Cluster-randomized trial, Three periods: Baseline (April through November 2005), Randomization and implementation (December 2005 through February 2006), and Intervention (March through August 2006)	5434 admissions to 10 intervention ICUs 3705 admissions to eight control ICUs	MRSA VRE	Surveillance cultures were obtained for MRSA and CRE colonization from patients in all participating ICUs; the results were reported only to ICUs assigned to the intervention In intervention ICUs, patients who were colonized or infected with MRSA or VRE were assigned to care with contact precautions; all the other patients were assigned to care with universal gloving	The intervention was not effective in reducing the transmission of MRSA or VRE The use of barrier precautions by providers was less than what was required The turnaround time for reporting a positive result on a surveillance culture was prolonged
Cepeda JA, et al., 2005 [5]	Multicenter, 1-year Prospective Study conducted in 3 ICUs (Medical and Surgical)	Admitted Patients *N* = 1676 Included *N*: 866	MRSA	Nose or groin swabs obtained within 24 h of admission, once a week and at discharge In the middle 6 months, MRSA-positive patients were not moved to a single room or cohort nursed unless they were carrying other MDROs	Transfer of MRSA-colonised or infected patients into single rooms or cohorting did not reduce cross-infection
Derde LPD, et al 2014 [8]	Multicenter (conducted in 13 ICUs), interrupted time series study (phase 2), followed by a cluster randomized trial (phase 3) A 6-month baseline period was performed before phase 2 (phase 1)	1st phase Screened *N* = 3215 Analyzed *N*: 1962 At Risk for MDR colonization: 1688 2nd phase Screened *N* = 3345 Analyzed *N*: 1926 At Risk for MDR colonization: 1681 3rd phase (conventional screening) Screened *N* = 3710 Analyzed *N*: 2280 At Risk for MDR colonization: 2029 3rd phase (rapid screening) Screened *N* = 4120 Analyzed *N*: 2351 At Risk for MDR colonization: 2007	HRE VRE MRSA	Chromogenic screening for HRE, MRSA and VRE (conventional screening) PCR screening for MRSA, VRE (rapid screening) ICUs were randomly assigned to either conventional screening or rapid screening [PCR testing for MRSA and VRE and chromogenic screening for highly resistant Enterobacteriaceae (HRE)]; with contact precautions for identified carriers	Mean hand hygiene compliance improved from 52% in phase 1 to 69% in phase 2, and 77% in phase 3 A decrease in trend of acquisition of antimicrobial-resistant bacteria in phase 2 was largely caused by changes in acquisition of MRSA In the context of a sustained high level of compliance to hand hygiene and chlorhexidine bathings, screening and isolation of carriers did not reduce acquisition rates of multidrug-resistant bacteria, whether or not screening is done with rapid testing or conventional testing

Table 1 (continued)

Author, Year	Setting design	Study Size	Target organisms	Intervention	Main outcomes
Ledoux G, et al 2016 [10]	Prospective, before-after study, conducted in a mixed ICU, during two 12-month periods 1-month 'wash-out' period interval	*N* = 1221 1st period *N* = 585 2nd period *N* = 636	*A.baumannii* Ceftazidime or Imipenem-resistant *P. aeruginosa* ESBL-GNB MRSA *S.maltophilia* VRE	Nasal and Rectal swabs, Tracheal Aspirate in intubated or tracheostomized patients obtained on admission and once a week During 1st period: systematic isolation performed in all patients at ICU admission During 2nd period: patient isolation performed when at least one risk factor for MDRO was met	Targeted isolation of patients at ICU admission was not inferior to systematic isolation, regarding the percentage of patients with ICU-acquired infections related to MDR bacteria [85 of 585 (14.5%) vs. 84 of 636 (13.2%) patients, risk difference,− 1.3%, 95% confidence interval (− 5.2 to 2.6%)]
Djibré M, et al 2017 [11]	Single-Center, Observational Study performed in patients admitted to MICU and SICU during 2 consecutive 6-month periods	1st period Screened *N* = 413 Included *N* = 327 2nd period Screened *N*: 368 Included *N* = 297	CRE ESBL (very low infection rate of MRSA and VRE in this Unit)	Rectal swabs were obtained on admission and once a week Universal screening for MDRO carriage and ACPs during the first 6-month period During the second 6-month period screening was maintained, but ACP were enforced in the presence of at least 1 defined risk factor for MDRO	The rate of acquired MDRO (positive screening or clinical specimen) was similar during both periods (10% [*n* = 15] and 11.8% [*n* = 15], respectively; *p* = .66) A targeted isolation screening policy on ICU admission was safe compared with universal screening and isolation regarding the rate of ICU acquired MDRO colonization or infection
Studies assessing safety and adverse events with the application of contact isolation					
Zahar JR, et al 2013 [12]	Based on the database of latroref III (a multicenter cluster-randomized clinical trial, testing the effects of MFSP, NCT00461461) Two centers included	Screened *N* = 1221 Included *N* = 1150 Isolated patients: 170 Non- isolated patients: 980	GNB MRSA VRE	A subdistribution hazard regression model with careful adjustment on confounding factors was used to assess the effect of patient isolation on the occurrence of medical errors and adverse events	After adjustment of confounders, errors in anticoagulant prescription [subdistribution hazard ratio (sHR) = 1.7, *p* = 0.04], hypoglycaemia (sHR = 1.5, *p* = 0.01), hyperglycaemia (sHR = 1.5, *p* = 0.004), and ventilator-associated pneumonia caused by MDRO (sHR = 2.1, *p* = 0.001) remain more frequent in isolated patients
Searcy R.J., et al 2018 [13]	Single-Center, Retrospective Chart Review of patient on MV receiving MRSA nasal screening and sedated within 24–48 h of ICU admission	Screened *N* = 389 Included *N* = 226 MRSA-positive: 114 (contact isolated) MRSA negative:112	MRSA	Nasal PCR assay Calculation of rate of inappropriate sedation, length of ICU stay, length of time on MV, and incidence of ventilator-associated complications	Patients placed on CI spent longer in the ICU (10.4 vs. 6.8 days, *p* = 0.0006), longer on MV (8.98 vs. 4.81 days, *p* < 0.001), and required a tracheostomy more frequently (37 (32%) vs. 14 (13%), *p* = 0.0003)

demands, particularly in settings where effective standard precautions are in place [9].

Ledoux et al., in a before–after single-center non-inferiority study, showed that a targeted isolation strategy at ICU admission was not inferior to a systematic isolation strategy regarding ICU-acquired infection related to MDRO (including key resistant both Gram-positive and -negative pathogens). With the targeted approach, CI was avoided in

Table 1 (continued)

Author, Year	Setting design	Study Size	Target organisms	Intervention	Main outcomes
Other studies (mathematic models etc.)					
Sypsa V et al., 2012 [7]	Prospective observational study conducted in a surgical unit of a tertiary-care hospital Surveillance culture for CPKP were obtained from all patients upon admission and weekly thereafter	Screened $N=850$; 18 patients were colonized with CPKP on admission and 51 acquired CPKP during hospitalization	Carbapenemase-producing Klebsiella pneumoniae	The Ross-Macdonald model for vector-borne diseases was applied to obtain estimates for the basic reproduction number R0 (average number of secondary cases per primary case in the absence of infection control) and assess the impact of infection control measures on CPKP containment in endemic and hyperendemic settings	The use of surveillance culture on admission and subsequent separation (mostly cohorted, less often in single room CI) of carriers from non-carriers coupled with improved hand hygiene compliance and contact precautions may attain maximum containment of CPKP in endemic and hyperendemic settings; it was estimated that in periods where R0 is 2, hand hygiene compliance should exceed 50% in order to attain an effective reproduction number below unity
Dhar S et al., 2014 [14]	Prospective cohort study Eleven teaching hospitals	1013 observations conducted on HCP	Not applicable	Compliance with individual components of contact isolation precautions and overall compliance (all five measures together) during varying burdens of isolation	Compliance with all components was 28.9%. As the burden of isolation increased (20% or less to greater than 60%), a decrease in compliance with hand hygiene (43.6–4.9%) and with all five components (31.5–6.5%) was observed

ACP additional contact precautions, *CI* contact isolation, *CRE* carbapenem-resistant *enterobacteriaceae*, *ESBL* extended spectrum beta-lactamase, *GNB* gram-negative bacilli, *HCP* health-care personnel, *HRE* highly resistant *enterobacteriaceae*, *ICU* intensive care unit, *MDRO* multi-drug resistant organism, *MFSP* multifaceted safety programs, *MICU* medical intensive care unit, *MV* mechanical ventilation, *MRSA* methicillin-resistant *Staphylococcus aureus, NICU* neonatal intensive care unit, *SICU* surgical intensive care unit, *VRE* vancomycin-resistant enterococci

almost one-third of patients [10]. In another sequential single-center observational study in a surgical ICU, the authors showed that a targeted isolation screening policy on ICU admission was safe compared with universal screening and isolation, resulting in similar rates of ICU-acquired MDRO colonization or infection during both study periods [11].

On the other hand, many studies have shown an increased rate of undesirable adverse events associated with CI [3]. In a study comparing the frequency of adverse events according to the isolation status in an ICU cohort population, the authors found five medication errors or adverse events that were significantly more frequently observed in patients under strict isolation: hypoglycaemia, hyperglycaemia, errors in administration of anticoagulants and ventilator-associated pneumonia (VAP) due to MDRO [12]. Searcy et al. showed that CI for MRSA colonisation was associated with over-sedation, prolonged ICU stay and mechanical ventilation [Searcy] [13].

Isolation capability varies across countries and settings. Dhar et al. showed that as the need for isolation is increasing, compliance with other measures is decreasing. There was a threshold of 40% for isolation within the unit, above which compliance with CI precautions (particularly hand hygiene) dropped significantly [14]. In a mathematic model, Gurieva et al. have shown that isolation capability is a major determinant of cost-saving curves. Targeted patient screening (based on previous carrier status) combined with screening of ICU-patients was the most cost-effective strategy when associated with an isolation capability of 25%. Better isolation capability is expected to render more extended screening strategies cost saving [15]. Therefore, CI local recommendations should be balanced on these issues.

We are convinced that CI will remain an important aspect of infection control, yet not the holy grail. Scientific evidence questioning its pivotal role particularly in the multifactorial arena of MDR-GNB persistence, permit us to state: "Less CI", is probably "more" in the ICU setting. Targeted and locally adapted contact isolation practices can avoid undesired adverse events in the patient's management, spare healthcare financial and human resources to be allocated in other preventive components, and obviate patient-family stress.

Its contribution in contemporary medicine cannot be viewed without rapid screening tools to be applied to targeted group of patients and certainly without strictly supervised hand hygiene. However, purpose-constructed studies are required to verify actual ranking of infection control components in each epidemiologic milieu.

Electronic supplementary material
The online version of this article (https://doi.org/10.1007/s00134-020-06173-5) contains supplementary material, which is available to authorized users.

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Compliance with ethical standards

Conflicts of interest
Dr. Poulakou reports personal fees from MSD, personal fees from Pfizer, personal fees from Biorad, personal fees from Menarini, personal fees from Angelini, outside the submitted work. Dr. Nseir reports personal fees from MSD, personal fees from Pfizer, personal fees from Gilead, personal fees from bioMérieux, personal fees from Bio-Rad, outside the submitted work. Dr. Daikos reports grants and personal fees from Pfizer, personal fees from Menarini, personal fees from MSD, outside the submitted work.

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