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State of the Science Review

Increased evidence for no benefit of contact precautions in preventing extended-spectrum β -lactamases-producing *Enterobacteriaceae*: Systematic scoping review

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Key Words:

Antimicrobial resistance
Contact isolation
Health care-associated infection
Standard precautions

Introduction: Extended-spectrum β -lactamases-producing *Enterobacteriaceae* (ESBL-E) is a critical antimicrobial resistance pathogen, to which we need to pay the greatest attention. This study was aimed at uncovering the present evidence for the preventive effectiveness of contact precautions for patients colonized or infected with ESBL-E.

Methods: According to the Preferred Reporting Items for Systemic Reviews and Meta-analyses (PRISMA) Extension for Scoping Reviews, we searched MEDLINE for articles with relevant keywords from the beginning of 2010 to October 18, 2022.

Results: Of the 355 articles found, 9, including 8 observational studies and 1 randomized controlled trial, were selected. Safety of discontinuing contact precautions was evaluated mainly in acute-care and long-term care hospitals. Consistently, all authors concluded that contact precautions can be safely discontinued in patients colonized or infected with ESBL-E.

Conclusion: The clinical impact of discontinuing contact precautions for patients with ESBL-E is minimal and can be safely withdrawn at acute, noncritical, adult care wards. Relevant data from pediatric and geriatric wards, as well as intensive care units, were insufficient and should be investigated in future research.

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In this era of antimicrobial resistance (AMR), increasing attention is being paid to infection prevention and control (IPC) strategies at health care facilities.¹ Global spread of AMR poses a great threat to public health worldwide, with growing clinical, social, and economic burdens.² Once health care-associated outbreaks by AMR bacteria develop, containment costs and productivity loss would soar to an unignorable extent,³ prompting the requirement of building a comprehensive system to prevent the AMR outbreaks from peacetime. AMR bacteria prevail through contacts among patients, health care

workers, and hospital environmental; therefore, contact precaution or isolation policies have been generally recommended to reduce the probability of its spread in hospitals.^{4,5}

Contact precautions are complexed countermeasures, consisting of single-room isolation, designated use of medical equipment, information sharing among health care workers, and universal application of personal protective equipment. They compel laborious and time-consuming burdens to health care workers, particularly nurses.^{6,7} This negative aspect of contact precautions potentially leads to delays in patient care,⁸ resulting from reduced visits to and less direct contact with patients by health care workers.^{9–11} Even various adverse consequences, such as increased events of falls and pressure ulcers, may affect patients under contact precautions.¹² Additionally, psychologic distress or disrupted mental well-being, including depression, anxiety, and even anger, may occur in isolated patients,^{7,12–15} finally leading to decreased patient satisfaction.¹⁶ A recent qualitative study highlighted that contact precautions negatively affected children as well.¹⁷ To mitigate the mental stress of such isolated patients, the isolation-coping program delivered by an infection control nurse

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Author contributions: H.H. conceived the study, searched related literature, assessed the quality of the studies, and drafted the manuscript. F.O. revised the manuscript and supervised the study.

was recently developed.¹⁸ Economic burdens resulting from contact precautions are also not ignorable.^{19,20} Accordingly, regarding unnecessary contact precautions, “too much is as bad as too little”, and understandably, increasing opinions for stopping contact precautions from bedside are rising in the literature.²¹

This paradigm shift from credulity in the preventive effectiveness of contact precautions to reconsideration of the burdensome measures is getting appreciated. With accumulations of clinical evidence, recent systematic literature reviews along with meta-analyses have concluded that contact precautions for methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococci* are no longer of help in reducing nosocomial infections and can be eliminated from routine care of such patients in hospitals.^{22,23}

According to the World Health Organization, extended-spectrum β -lactamase-producing *Enterobacteriales* (ESBL-E) are listed as a critical AMR pathogen that require urgent countermeasures with a higher priority to be tackled with.²⁴ Despite global actions to stop ESBL-E dissemination, they have spread in the community as well as nosocomial settings.²⁵ Historically, in hospitals, contact precautions were strongly endorsed for patients with ESBL-E colonization or infection to reduce the risk of nosocomial spreading.^{4,5} Increased isolations of ESBL-E in health care settings poses a therapeutic challenge and increases the rate of carbapenem administration, a drug of last resort. However, clinical significance of contact precautions in preventing ESBL-E incidence in health care settings has remained inconclusive.²⁶ Negative data regarding this established consensus have been reported, and *pros* and *cons* discussion has arisen in these years.²⁷ Practically, as of 2014, mainly because of the lack of staffing and isolation rooms, only 68% of IPC providers from European countries had considered contact precautions necessary for ESBL-E.²⁸

As far as we concern, no authenticated guideline that publicly allows cessation of contact precautions exists for inpatients colonized or infected with ESBL-E.²⁹ Single-bedroom contact isolation is unnecessary according to a recent cluster-randomized, crossover study.³⁰ Heavy burden on health care workers of excessive contact precaution merely results in lower compliance.³¹ Therefore, establishment of an evidence-based contact precaution approach is highly required. The present study was aimed at summarizing the present evidence for the preventive effectiveness of contact precautions for patients with ESBL-E following the systematic scoping review approach.

METHODS AND DATA

Study design and strategy

We performed a systematic scoping review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews (Appendix 1).^{32,33} MEDLINE was searched for all peer-reviewed articles from the beginning of 2010 to October 18, 2022, with following searching terms: “Extended-Spectrum Beta-lactamase”(All Field) AND “discontinuing contact precautions” (All Field) OR “discontinuation of contact precautions” (All Field) OR “contact precautions cessation” (All Field) OR “cessation of contact precautions” (All Field) OR “Contact isolation” (All Field). No filters for the study design or language were employed. Along with the reference lists of all articles that met the eligibility requirements, other pertinent articles were screened.

Eligibility criteria

The inclusion criteria were as follows:

- (1) Articles describing the clinical effectiveness of contact precautions for inpatients with ESBL-E

- (2) Randomized controlled trials, case-control studies, cohort studies (prospective or retrospective), cross-sectional studies, case series, and case report

The exclusion criteria were as follows:

- (1) In vitro or animal experiments, conference or meeting abstracts, irrelevant topics, review articles, guidelines, and commentaries

Study selection, data extraction, and definition

H.H. analyzed selected articles for full-text evaluation, and those deemed appropriate for this study underwent a thorough evaluation. The following data were collected from each study using a standard data collection form in accordance with PRISMA and Cochrane Collaboration criteria for systematic reviews: name of the first author, year of publication, country of origin, study design and period, aim of the study, study population, comparative group, key findings, and limitations.

RESULTS

Search results and study selection

Figure 1 shows the stages for locating, screening, evaluating eligibility, and incorporating or excluding research following a PRISMA flow diagram. The initial search of MEDLINE databases detected 355 articles. Of these, 338 papers were removed because they dealt with irrelevant topics. Subsequently, 17 articles were further screened for eligibility and 8 were additionally excluded from the study. Finally, 9 articles were selected for the final review.

Description of observational studies

Overall, 8 observational studies were identified (Table 1).^{34–41} First, a study incorporated with a stochastic transmission model suggested that, in settings with an increased number of sporadic sources for ESBL-E from the community, contact isolation would not contribute to reducing ESBL-E rates in hospitals.³⁴ Subsequently, Tschudin-Sutter et al.³⁵ conducted a prospective, observational study to validate the cessation of contact precautions for patients with ESBL-E both in acute-care and long-term care (geriatric/rehabilitation) hospitals. The transmission rates of ESBL-E were 2.6% and 8.8%, respectively, which did not differ from those reported during the period before discontinuation of contact precautions. Moreover, cessation of contact precautions did not increase the incidence of ESBL-E or infectious episodes outside the developed countries.³⁶ Discontinuation of contact precautions did not increase ESBL-E acquisition among patients managed at an intensive care unit in France.³⁷ Single-centered^{38–40} and small-sized multicentered studies⁴¹ repeatedly reported the same results.

Description of randomized controlled trials

Only one randomized controlled trial was performed at 20 non-critical care adult wards of 4 European countries in a form of a cluster-randomized crossover design.⁴² The authors concluded that contact precautions were not superior to standard precautions in reducing the incidence or incidence density of ward-acquired ESBL-E cases. The results remained similar when stratified by species (ESBL-producing *E. coli* and ESBL-producing *Klebsiella pneumoniae*). Moreover, incidences of ward-acquired ESBL-E infections were statistically at the same level during contact and standard precaution periods.

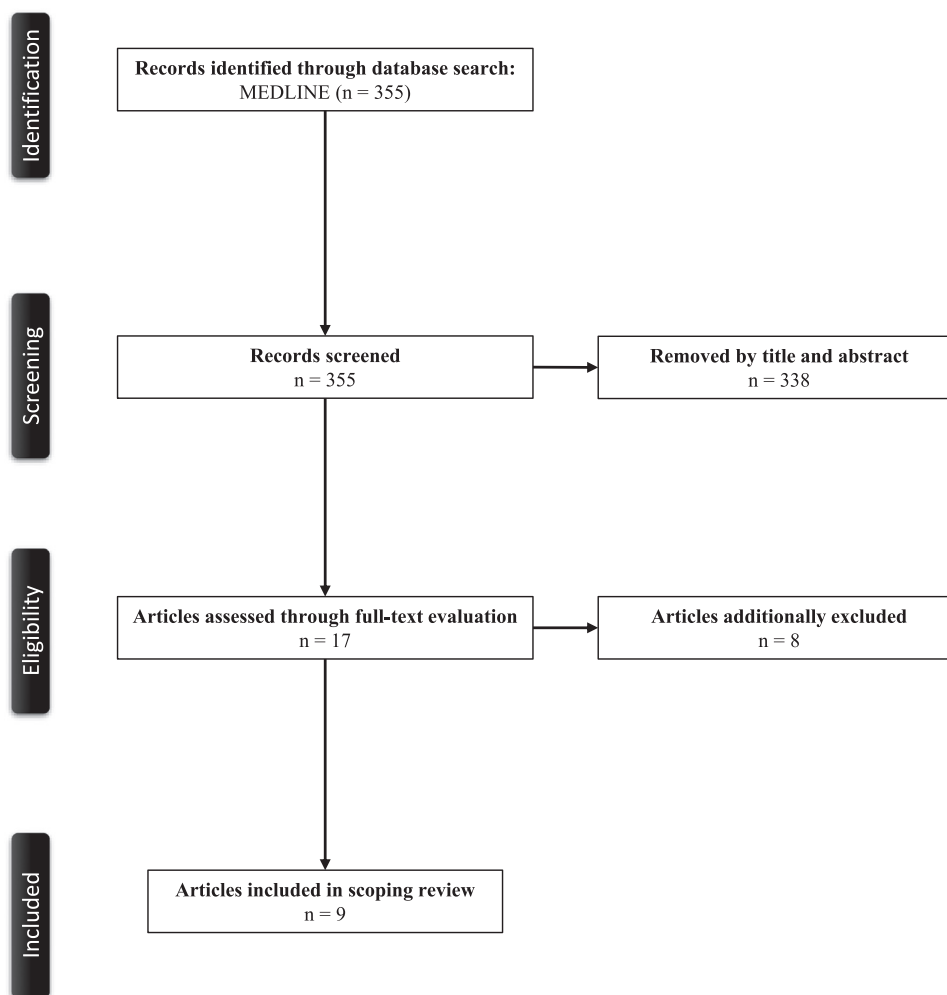


Fig 1. Flowchart of the study process.

DISCUSSION

We conducted a systematic scoping review to uncover the updated evidence of the clinical significance of contact precautions in preventing and reducing ESBL-E isolations and infections among inpatients. Consequently, we detected 9 relevant articles from 2013 to October 18, 2022. In addition to these, we found 1 retrospective observational study conducted at 2 university hospitals in France, which adopted distinct patient isolation policies (contact or standard precautions) for ESBL-E carriers. This study revealed no increase in ESBL-E isolation.⁴³ A preprint literature based on an interrupted time series analysis supported similar conclusions.⁴⁴ Consistently, all authors concluded that contact precautions could be safely discontinued in patients colonized or infected with ESBL-E.

These accumulated clinical data suggest avoiding contact precaution policies for ESBL-E-positive patients with an increasing consensus worldwide. Tschudin-Sutter et al.^{35,45} have contributed to starting this discussion by reporting that ESBL-E transmission rates before and after contact precaution cessation at a Switzerland university hospital did not differ significantly (1.5%⁴⁵ vs 2.6%³⁵). Subsequent to several observational studies, the cluster-randomized crossover study published in 2020 corroborated this finding.⁴² The incidence of ward-acquired ESBL-E cases per 100 cases in contact and standard precaution periods were both 6.5, with an unadjusted estimated rate ratio of 0.99 (95% confidence interval [CI]: 0.86–1.14). Moreover, the incidence density of colonization with ESBL-E, which was defined as

the ESBL-E positive rate per 1,000 patient days at risk at the ward level among those who stayed for over 1 week, did not differ significantly (6.0 events per 1,000 patient days during contact precaution periods and 6.1 during standard precaution periods), with unadjusted estimated rate ratio of 1.00 (95% CI: 0.90–1.11). The incidence density of ward-acquired ESBL-E infections did not differ significantly (0.16 per 1,000 patient days in contact precautions vs 0.27 in standard precautions), with an unadjusted estimated rate ratio of 1.00 (95% CI: 0.61, 0.32–1.12).

Rational and important points for the clinical safety of abandoning contact isolations for patients with ESBL-E colonization should be addressed. First, compared to gram-positive organisms, such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococci* species that survive on environmental surfaces for even weeks, *Enterobacteriaceae* cannot endure dried conditions.^{46,47} In a previous cohort study, the estimated spreading rate of ESBL-E was 1.5% (2/133 contact patients) even among intensive care unit patients supposed to be at a high risk of cross-contaminations.⁴⁵ Second, the importance of high adherence to standard precautions and hand hygiene should be highlighted. Preceding data from Switzerland may promise the validity of contact precautions-free patient care.^{35,45} However, their compliance to these basic infection prevention skills was high, particularly for hand hygiene with a compliance rate of over 90%.^{5,48} Hence, when IPC practitioners are about to change their contact precaution policy for ESBL-E carriers at their hospitals, they need to evaluate their hand hygiene compliance in advance. Third,

Table 1
Main characteristics of the 9 observational studies

First author y, country	Study design (period)	Aim	Study population	Comparative groups	Key findings	Representative limitations of the study
Domenech de Cellès 2013, France	Single-centered, retrospective observational study utilizing a stochastic transmission model (Jun 2009 to Jul 2010)	To clarify the role of contact isolation in preventing ESBL-E spread and predicting effective interventions in various settings	All single-room isolated patients with ESBL-E colonization or infection diagnosed during the stay or up to 2 days after discharge from the pediatric ward	Those with ESBL-E colonization or infection a cohorted in an 8-bed unit	Contact isolation alone may not suffice to substantially reduce ESBL-E rates in hospital settings. Countermeasures against sporadic sources and patient-to-patient transmission would reduce the ESBL-E incidence.	Limited assumption in the mathematical model Testing sensitivity to detect ESBL-E carriage Internal validity (hygiene enhancement program implemented concomitantly)
Tschudin-Sutter 2016, Switzerland	Two-centered (university hospital and long-term care center), prospective observational study (Jan 2012 to Dec 2013)	To validate the cessation of CPs for patients infected or colonized with ESBL-E in different settings	All contact patients who shared the room with an index patient with ESBL-E for at least 24 h	None	Transmission rates of ESBL-E were 2.6% and 8.8% at an acute-care and a geriatric/rehabilitation hospital, respectively, similar to that reported during the period before discontinuation of CPs.	Underestimation due to only one screening and absence of rectal swabbing Overestimation by inclusion of community-derived ESBL-E isolates
Metan 2017, Turkey	Two-centered, observational study (2015 and 2016)	To determine the results of abandoning CPs for ESBL-E carriers	Patients hospitalized at a tertiary care center and an oncology hospital in 2016	Patients hospitalized in the same hospitals in 2015	Infection density or bacteremia rates did not increase for ESBL-E after cessation of CPs.	Not comparing the types of ESBL-E infection (bacteremia only) Absence of a molecular epidemiology analysis
Renaudin 2017, France	Single-centered, prospective noninferiority, before-and-after study (Jan 2012 to Feb 2016)	To compare incidence densities of ESBL-E acquisition at ICUs before and after discontinuation of CPs	Patients admitted to the ICU during CPs periods (1,547 cases; Jan 2012 to Jan 2014)	Patients admitted to the ICU during SP periods (1,577 cases; Feb 2014 to Feb 2016)	Discontinuing CPs did not increase ESBL-E acquisition (2.7 and 2.1 cases per 1,000 patient days in CPs and SP periods) at ICUs.	Single-center study Difficult to determine the causality
Thompson 2020, United States	Single-centered, prospective before-and-after study (Jan 2014 to Aug 2017)	To investigate incidence rates of health care-associated ESBL-E infections and colonization before and after eliminating CPs	Patients hospitalized during the CPs period (Jan 2014 to Nov 2015)	Patients hospitalized during the SP period (Dec 2015 to Aug 2017)	The incidence of ESBL-E infections in CPs and SP periods did not differ significantly (3.71 and 3.00 per 10,000 patient days).	No screening for ESBL colonization on admission No background data to review detailed patient comorbidities or other clinical factors No genetic typing
Hernández-García 2020, Spain	Single-centered, prospective before-and-after study as a part of the R-GNOSIS project (Mar 2014 to Mar 2016)	To assess the benefit of CPs over SP in preventing nosocomial transmission of ESBL-E isolates	Patients hospitalized during the CPs period (Mar 2014 to Feb 2015)	Patients hospitalized during the SP period (Apr 2015 to Mar 2016)	CPs measures were not effective in reducing ESBL-E transmission.	None clearly mentioned
Maechler 2020, Germany	Multicentered (20 wards from 4 European university hospitals), cluster-randomized crossover trial (Jan 2014 to Aug 2016)	To establish the benefits of CPs over SP in reducing the incidence density of ESBL-E colonization and infection at adult medical and surgical wards	Patients admitted to noncritical care adult wards during the CPs period (12 months)	Patients admitted to noncritical care adult wards during the SP period (12 months)	CPs was not superior to SP in reducing the acquisition of ESBL-E in noncritical care adult wards.	CPs might be insufficient to prevent transmission Limitations of the study design Inadequate sensitivity of screening tests Differences in the effect of CPs at the species level
Gottlieb 2021, United States	Single-centered, retrospective observational, quasi-experimental study (Oct 2016 to Aug 2018)	To describe the impact of discontinuing CPs for ESBL carriers	Patients hospitalized during the CPs period (Oct 2016 to Aug 2017)	Patients hospitalized during the SP period (Oct 2017 to Aug 2018)	No change in the prevalence of ESBL-E at the inpatient or emergency department after discontinuing CPs	Retrospective nature of the study raises the possibility of confounders. Differences in transmissibility of non <i>E. coli</i> ESBL-E should be investigated.
AbiGhosh 2021, Lebanon	Three-centered, cross-sectional study (Jul to Nov 2017)	To assess the effect of CPs on ESBL-E colonization rates among nurses	Nurses working at hospitals	None	Nurses working at a hospital with CP policy for ESBL-E carriers had less risk of colonization.	Low participation rate (36.7%) and unequal sample size among hospitals No genetic typing

ESBL-E, extended-spectrum β -lactamase-producing *Enterobacteriaceae*; CPs, contact precautions; ICU, intensive care unit; R-GNOSIS, Resistance in Gram-Negative Organisms: Studying Intervention Strategies; SP, standard precaution.

health care workers may in turn hesitate to cease contact precautions for ESBL-E carriers suddenly. In such a case, IPC practitioners may need to gradually set contact precautions apart from patient care while incorporating various opinions from medical staff.

Generalizability of the removal of contact precaution policies in ESBL-E harboring patients is a matter of debate, as discussed.³⁵ Nosocomial spreading of AMR pathogens, including ESBL-E, is associated with various clinical factors, such as person-to-person cross-transmission over longer periods (adherence to hand hygiene practice among both health care workers and inpatients), number or proportion of patients with such organisms (colonization pressure), and antibiotic consumption (selective pressure).^{49,50} Due to insufficient education and training for infection prevention skills and antimicrobial stewardship, long-term care hospitals for geriatric patients apply these factors and, therefore, are at a high risk of allowing nosocomial AMR outbreak. The transmission proportion of ESBL-E in geriatric rehabilitation hospitals were comparatively higher compared to acute-care hospitals: 8.8% in Switzerland³⁵ and 6.5% in Israel.⁵¹ Additionally, differences in environmental transmissibility among ESBL-producing *E. coli* and other ESBL-producing organisms should be considered.⁵² Despite contact precautions, the transmission rate of ESBL-producing *K. pneumonia* was higher than that of ESBL-producing *E. coli* (8.3% vs 4.5%).⁵³ The transmission events were significantly associated with longer duration (>5 days) of sharing the same room as an index ESBL-E-positive patient.³⁵ Thus, the contact precaution policy may be reasonable for patients expected to be admitted for prolonged periods, particularly when they depend on nursing care.

This review has some limitations. First, because of inaccessibility to other databases, such as EMBASE, we screened only MEDLINE for the search terms. This could have resulted in underestimation of the relevant articles. Second, a publication bias should be considered when evaluating the IPC topics; results of studies that could not identify the safety of discontinuing contact precautions might not have been published arbitrarily. Third, due to insufficient data, IPC policy changes for ESBL-E carriers at pediatric or geriatric facilities should be individually assessed. Future research, preferably in the form of randomized controlled trials, should focus on these medical situations. Fourth, most eligible studies have been performed in situations with well-equipped single rooms and good antibiotic stewardship. Therefore, whether this applies to other resource-poor environments, such as those in Asian and African countries, should be verified in future studies. Finally, we did not perform a quality assessment of the article selected. This is because there is no guideline or guidance on scoping review that instructs quality checks for the risk of bias in the included articles. Actually, a previous scoping review for the scoping reviews articles revealed that only 14% of published scoping reviews articles conducted the quality assessment.⁵⁴

CONCLUSION

Collectively, despite these concerns, our review of the existing evidence endorsed that the clinical significance of discontinuing contact precautions for patients with ESBL-E is minimal and can be safely withdrawn at acute, noncritical, adult care wards. Due to lack of relevant data from pediatric, geriatric, and intensive care wards, universal removal of contact precautions for patients with ESBL-E cannot be recommended. Appropriate cessation of contact precautions would save medical resources, such as personal protective equipment, additional costs and time, potentially result in improvement in patient care and reduction in psychological distress of isolated patients.

APPENDIX 1

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3-5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (eg, population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	5
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (eg, a Web address); and if available, provide registration information, including the registration number.	6
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (eg, years considered, language, and publication status), and provide a rationale.	6, 7
Information sources*	7	Describe all information sources in the search (eg, databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	6
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	6, 7
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	7
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (eg, calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	7
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N/A
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	7
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	7, 8

(continued)

(Continued)

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	8
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	N/A
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	8-9, Table 1
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	8-9, Table 1
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	9-12
Limitations	20	Discuss the limitations of the scoping review process.	13
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	13
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	14

JB1 = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

*Where sources of evidence (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

[†]A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (eg, quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with information sources (see first footnote).

[‡]The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

[§]The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (eg, quantitative and/or qualitative research, expert opinion, and policy document). From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med*. 2018;169:467–473.

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